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From

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127 W. 9th St.

Cincinnati

GUIDE

TO THE

Examination of Urine,

WITH SPECIAL REFERENCE

TO THE

DISEASES OF THE URINARY APPARATUS,

—BY—

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PREFACE.

In bringing this little work before the medical public, the translator has been encouraged by the fact of its popularity on the Continent, and its nearly universal adoption by the German high-schools. Now that the second German edition has appeared, considerably altered from the first, as well as enlarged, he no longer hesitates in bringing it before the profession of this country. As the authors state in the preface to the first edition, this book is not intended for the physiological chemist, nor for him who is going to make animal chemistry a specialty; neither does it supply the place of many larger works, such as exist in the English language. Every test, every method, is brought home to the student and physician for use in practice. A great amount of space and time is spent upon methods, showing how an examination of urine and diagnosis of disease can be most readily and quickly made. The book, in every respect, is fully up to the times, for which the names of the authors, alone, are sufficient guarantee.

The office of the translator has been not only to translate, but, also, in several places, to make slight additions or omissions, being guided therein by his experience as teacher of urinalysis in the Medical College of Ohio. In addition, he has supplied the illustrations, that have been drawn by his student, Mr. W. S. Christopher, and which, he hopes, will make the book more attractive, as well as more instructive, than it would have been in the German form.

"May the endeavors to increase the utility of this work not be without result."

F. F.

INTRODUCTION.

The results of those processes, usually complicated, which go to make up the basis of organic life, are, on the one hand the building up of the body; on the other, changes which have been collectively termed "retrograde metamorphosis." The effete substances which can no longer be utilized by the economy are eliminated by the skin and lungs (in the form of gas); by the intestinal tract and kidneys (either in the form of solids or in solution).

In order to come to a correct conclusion regarding the nutrition of the body (the normal or diseased process), both the functions of the above named organs and the conditions of the excrementitious matter furnished by these must be equally carefully examined into. In the healthy condition of the organism this is connected with immense difficulties and in any material disease becomes entirely impossible.

The physician is compelled to restrict his examination to one of these excretions, if he wishes to gain an insight into the economy, but he can examine the most important excretion—the urine.

The urine, at least, registers approximately, by means of qualitative and quantitative changes the variations of histological processes. In addition, the examination of urine has this advantage, that the fluid can be collected without diffi-

culty and its analysis, so far as it interests the practicing physician, can be carried out by very simple means.

The kidney, as it is not a lifeless filtering apparatus, will be subjected to disease, and as a result of these pathological changes, substances will be mixed with the urine whose presence alone will lead the physician to a diagnosis of the disease. The urine, then, gives us a general insight into the condition of the whole body, but especially into the condition of the urinary apparatus. In passing, it is only necessary to mention, that, on account of the fact, that many substances have the peculiarity of leaving the organism after having remained in it for a variable length of time, by means of the kidney; the urine is of great importance to the physiologist, the phamaceutist and in some instances to the expert in medico-legal cases.

The desire to recognize disease from the appearance of the urine reaches back into the most remote past of scientific medicine. In his precise and objective observation of the sick, Hippocrates did not disregard the changes in the urine. He taught, in accordance with the condition of other sciences, his pupils the semiotic and also, prognostic importance of these changes. He demonstrated the physical properties of urine; the quantity, color and clearness, the cloudy or turbid appearance; the apparent differences in the sediments and referred these to diseases of the urinary apparatus. He even tried to show the influence of food and drink upon the condition of the urine.

We therefore find in the descriptions of disease of Greek authors, after him, the condition of urine taken into consideration, without their having deviated from the opinions of the great Coic physician. Since Galen developed the teachings

of Hippocrates, and treated them systematically, these have been considered as absolutely true. Observations on urine for a long time did not show any progress.

Throughout the following centuries rarely is an author found, who, through personal observations, added anything to these writings. To the Arabian Iben Sina (980—1037) usually called Avicenna, belongs the credit of having pointed out that various external causes, such as fasting, vigils, physical and mental exertions, have an influence upon the condition of the urine. He also demonstrated that drugs taken internally may cause a temporary discoloration of the urine. Otherwise the Arabic physicians did nothing of importance on this subject, notwithstanding the presence of an uroscopist at every court throughout the orient.

The most prominent author on our subject, that lived in ancient times or during the middle age, is beyond doubt Johannes, called Actuarius, who flourished in the thirteenth century at the court of Byzantium. Combining his own experience with the observations of the school of Hippocrates-Galen, he describes the physiological and pathological changes in urine in seven books of his work, "περὶ οὔρων" to their most minute details. In addition, he is quite conspicuous on account of his methodical and clear descriptions. This production, which exhausted everything that could be expected in the then condition of the allied sciences and methods, remained so isolate, found so few followers, that this division of symptomatology was neglected more and more in the time following this work. How far degeneracy had taken place, can be seen that it furnished material for satirical representations in the Dutch genre pictures, as well as for many comedies of Moliere and other poets.

As the ideas up to this time, on the chemical composition of the urine were highly defective, the external appearance only could be considered by all old authors. Real progress could only be expected at a time when chemistry and its methods of examination had arrived at a certain degree of development. With Lorenzo Bellini of Florence this progress begins.

Bellini evaporated urine and observed, that as he again added water, the solids would again dissolve, returning gradually, step by step, through various intensities of taste and color, nearly to the original condition. From this, he concluded that the different color and taste of urine depended upon the relation the solid constitutents bore to the water, a conclusion, upon which, even at the present, the scale of colors of Vogel is based.

Many important chemical discoveries followed soon after this. Willis discovered sugar in urine; Brandt discovered phosphorus, which Markgraff stated, came from the phosphates that were contained in the urine.

Rouelle, the younger discovered urea in 1773 and found that calcic carbonate was present in the urine of herbivora, as well as a substance related to the flowers of benzoe (Hippuric acid). In 1770 Cotugno found albumen in urine, in 1798 Cruickshanc connected this discovery with dropsy and in 1807 Bright, finally demonstrated the connection between diseased kidneys and albuminuria.

At the same time chemical analyses of gravel and calculi were undertaken. Among the many publications of merit, on this subject, those of Scheele, Wollaston, Wetzlar and Prout must be especially mentioned.

Two Frenchmen, however, have furthered the develop-

ment of uroscopy, to its present point, more than any one. The researches of Rayer that are put down in the large work "Les maladies des reins," are the foundations for our present knowlege of kidney diseases. Becquerel, the son of the celebrated physicist, had for a long time, occupied himself with urinalysis under the direction of Andral, and in a modest manner gives to him all the credit of having furnished the ideas for observations. These observations, extending through many years, he published in the work "Semiotique des urines." For the thirty years since the appearance of this book many observers have devoted themselves to this branch, so that, probably no other division of zoochemistry has so extensive a literature as this.

After this short sketch of the development of our subject, there remains only a brief discussion of the divisions that have been thought necessary.

After a chapter on the microscopic structure and function of the urinary organs, without a knowledge of which, comprehension of disease becomes an impossibility, the physical characters and chemical constituents of urine, *as far as they seem to us important to the practicing physician*, are treated of. Upon this follows a description of the microscopical part, *i. e.* the sediments of urine. Repetitions will be of advantage to the beginner, for whom this little work is intended.

The short key to the method of examination will also be of value to the beginner. Finally a description of the simple (uncomplicated) diseases of the urinary organs, will be found, in so far as they give signs that can be utilized for diagnosis.

CHAPTER I.

HISTOLOGY OF THE URINARY APPARATUS.

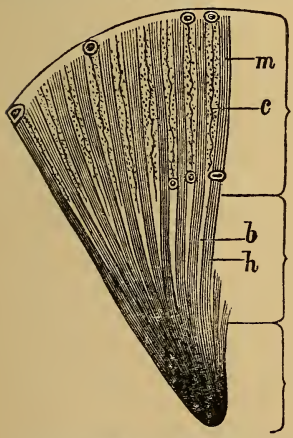
I. The Kidney.*

If a kidney be cut from the papilla to the fibrous capsules, two concentric layers become distinctly visible to the naked eye; the striped medulla and the peripheral, more granular cortical, the latter surrounding the former.

If the vessels and uriniferous tubes have previously been injected with different colors, other divisions can be made upon the section.

Fig 1.

A longitudinal section through the kidney of a dog; both blood vessels and urine tubes injected.



p, Papillary portion; *g*, border layer of the medulla; *r*, cortical layer. The dark stripes of the medulla, *h*, are bundles of uriniferous tubules, their continuation, *m*, into the cortex. The light divisions of the medullary layer, *b*, correspond to the bundles of blood-vessels of the border layer. The light portions of the cortical that are occupied by dots (glomeruli), *c*, demonstrate the position of the labyrinth (after Ludwig).

In the papilla, and in the neighborhood above it, the kidney seems to be uniformly striped, colored only by the mass injected

*The investigations of Kölliker, Schweigger—Seidel, and Ludwig were taken as basis for this description of histological relations.

into the urinary tubes; this division is called the papillary layer of the medulla. Above this there is a section which is also striped but which already begins to show the mass injected into the blood vessels. There can here be seen alternate stripes of both injection masses, arranged as radii, next to each other. This part is called the border layer of the medulla. The third, outer layer, finally, that encloses both the others, is called the cortical layer.

In the cortical layer itself, two substances can be distinguished that are arranged in the same radial way and that can be discerned by means of the two injected colors. The one is striped, and is colored by the mass that has been forced into the urine tubes, and is the direct continuation of the fibres of the medulla and is called medullary bundles, (pyramids of Ferrein.) The other substance shows granules principally, which seem to be colored by the mass injected into the blood vessels, and is the so-called labyrinth or cortical layer in the strict sense.

Accordingly we find when we take the microscope, that the papillary layer is made up principally, of straight uriniferous tubules; the border layer partly of straight uriniferous tubules, partly of straight blood vessels; the pyramids principally of straight uriniferous tubules, and finally, the labyrinth consists partly of convoluted tubules and partly of covoluted tubules and tortuous blood vessels.

This system of blood vessels and uriniferous tubules is supported by connective tissue which forms a very sparse stroma. This consists of a very fine network of connective tissue corpuscles and is better marked in the medullary layer than in the cortical. Upon the surface of the kidney the stroma condenses into a delicate membrane which is but

loosely connected with the fibrous investing membrane. The latter consists of ordinary connective tissue with a dense, fine, elastic network; it surrounds the whole kidney, and at the hilus, is directly attached to the vessels and the pelvis of the kidney.

The Uriniferous Tubules begin in the labyrinth. Each begins in the form of a spherical dilatation (Capsula Malpighii).

"This is continued through a contracted portion (the neck of the capsule) into a dilated tube, which takes its course in manifold curves towards the medullary portion. When this convoluted portion has reached the border layer, in the form of a wide tube, it suddenly becomes pointed, and penetrates as a straight narrow canal, more or less deeply, into the medullary substance (descending or closed limb of the loop) turns back in the form of a narrow loop (Henle's loop) and runs directly upward towards and into the cortical substance (ascending or open limb of the loop)".*

"Upon returning to the cortex the tubule does not seek the exact place from which it came; on the contrary, it seems to avoid the labyrinth and lies close to the nearest pyramid of Ferrein. Sooner or later it leaves its straight course again and enters in the form of more or less angular curvatures, as so-called intermediate portion, between the tortuous canals, the labyrinth. From here it returns, forming an arch whose convexity is directed towards the convexity of the kidney, towards the pyramid of Ferrein, to give up its individual course. The latter is accomplished, in that several tubules, coming from various directions to one point, are melted together for the formation of a wide and straight tube (collecting tubule)." This takes a straight course until

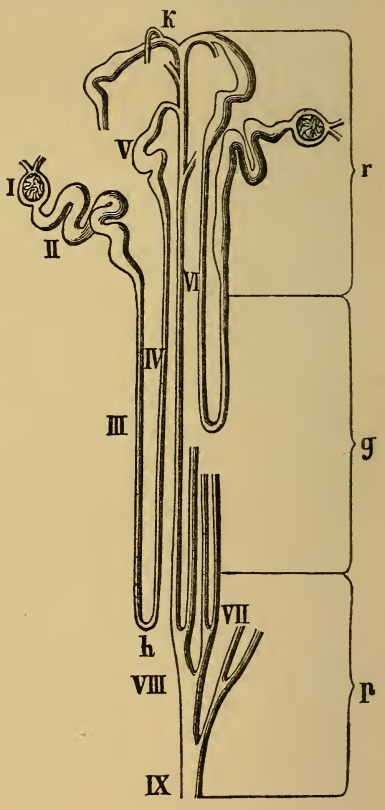
*The quotation is taken from the classic description of C. Ludwig. (Handbook of Histology, Stricker.)

it reaches the papillary portion of the kidney where it unites, dichotomously, with neighboring collecting tubules, and so on, until the uniting collecting tubules empty, in the form of the ductus papillaris upon the surface of the papilla.

p, Papillary layer; *g*, border layer of the medullary substance; *r*, cortical substance. Capsule of glomerulus I, which enters into tortuous portion II through the neck. This tapers at the boundary between medulla and cortical into the descending limb of the loop III, and, as such, goes through Henle's loop *h*, into the ascending limb of the loop IV. To this is added the intermediate portion V, which, through the external arch at the top of *r*, enters the collecting tubule. The collecting tubule unites with its neighbor of the same pyramid VII, to form the principal tube VIII, and this, finally unites with others to form the ductus papillaris IX.

Fig 2.

Schematic representation of the course of a uriniferous tube; human kidney.



The walls of the Malpighian capsule, like those of the blood and lymph capillaries, are made up of a mosaic of cells. The glomerulus, or tuft, is not washed directly by the fluid contents of this capsule; this is prevented by a layer of cells not distinctly separated from each other, containing spherical nuclei, that cover the external surface of the tuft of vessels. "From the neck of the capsule to the commencement of the papillary duct, the wall of the tubule is composed of a tunica propria and a layer of epithelium resting upon its inner surface." The tunica propria is homogeneous, vitreous, and elastic.

The epithelium, which invests the inner surface, consists of only one layer and possesses nuclei. The form of the nuclei is everywhere the same; they are spherical, sharply defined and their contents show many granules. The body of the cell however varies very much in regard to shape.

In the arched, tortuous tubules the epithelium forms a connected, gelatinous, cloudy mass, in which nuclei are imbedded at equal distances from each other. A division into cells, corresponding to these nuclei seems to be entirely absent.

"This epithelial pulp sits very loosely upon the basal membrane," and the whole substance can be easily forced out of the cut tubules in the form of a cylindrical mass. With the microscope there are discovered many oil globules, and also other dark corpuscles which, upon the addition of dilute acid are cleared up (cloudy swelling of the epithelium). After the clearing up with acids it is frequently impossible to distinguish anything distinctly except the nuclei of the cells.

"In the narrow tubules, which form the limbs of the loop of Henle, there appears, in the place of the dark and bulky epithelium, already described, a light and meager epithelium which lines the walls of the tubule with a layer that is considerably arched by the nuclei."

Beyond the loop of Henle, where the diameter of the tube increases, the epithelium looks as if it were made up entirely of cylindrical cells, that are arranged like the shingles of a house, placed over each other in the direction of the medullary to the cortical layer.

In the intermediate portion the gelatinous layer is again found.

"In the collecting tubules, to the papillary duct, the epithelium is made up of cylindrical cells; distinctly separated from each other, that rest with their base upon the tunica propria directing their blunted points toward the lumen of the tube.

The Blood vessels of the Kidney.—The renal artery sends the greater part of its blood through the cortical portion. Its branches penetrate, without forming a net-work, to the boundary of the cortex and divide, rapidly, into very minute arteries; the arteriolæ interlobulares and arteriolæ rectæ. The interlobular arterioles take their course between two pyramids of Ferrein where several primitive bundles meet. Arrived in the layer of tortuous tubules, they give to each Malpighian capsule a branch. This branch (Vas afferens glomeruli) perforates the spherical end of the tubule (according to other authorities it pushes the same before it), and here, terminates "in a pendulous bundle of capillaries, (glomeruli), that, in their turn, are collected, within the capsule, into one venous branch (Vas afferens glomeruli)."

This small branch has its exit, from the capsule, at the same place that the artery takes its entrance. After it has left the capsule, "it first, takes the direction towards its pyramid; or, where this is wanting (as in the outer layer of the cortical substance), directly toward the tortuous tubules and divides into a number of capillaries, that, immediately after their origin, combine to form a net-work," and in this way produce meshes that surround the uriniferous tubules. All the efferent vessels communicate with each other, by means of their capillaries, and in this manner form a continuous capillary net running through the whole cortical, which, in its turn, anastomoses with the meshes around the pyramids, in this way being in connexion with the capillaries of the medullary portion.

The arteriolæ rectæ, all of which enter the medullary part from the direction of the cortical "take their course in the slit-like spaces, that occur, at the border of the medullary part, between the tubules, and strive to reach the papillæ;" in that they divide into branches that run in a more parallel direction. Where these vessels come into contact with the convergent tubules, they divide into capillaries, that surround these, extending even to the papilla. These capillaries, as has been before mentioned, are connected with those of the cortical portion.

By these capillary nets, the venous trunks are originated. In the cortical portion, in that part in which no glomeruli are found, the union takes place in the form of stars (Venæ stellatæ.) The common trunk penetrates the cortical portion which is supplied with tufts and tubules, lies in the neighborhood of an interlobular artery, and takes up many veins coming from the cortical portion.

The veins of the medulla (venulæ rectæ) run in the spaces that are occupied by the arteries, and, at the border of the cortex, unite with the veins coming from these to form larger trunks.—The capsule of the kidney receives its blood-vessels partially, from the interlobular arteries, partially from other neighboring trunks (the phrenic, lumbar and supra-renal arteries). Their capillaries partly enter the stellate veins, partly veins corresponding to the arteries that have given the blood.

The *Nerves* of the kidney are derived from the coeliac plexus of the sympathetic. Their final terminations are not known. They follow the course of the larger vessels, as well as the lymphatics that enter the lumbar glands.

II. The Efferent Passages.

The *Ureters*, *Pelvis of the Kidney* and the *Calyces* are made up of an external fibrous membrane, a layer of unstriped muscular tissue, and a mucous membrane. The fibrous coat is continuous with the albuginea of the kidney and is made up of connective tissue and elastic fibres. In the ureters, the muscular layer, is distinctly made up of three divisions: the inner one runs longitudinally, the middle one transversely, and the outer, which is the thinnest, again longitudinally. In the pelvis the relations are the same, except in the calyces, the muscular layers become thinner and finally disappear where they touch the papillæ. The mucous membrane is thin, rather rich in blood vessels, without glands or papillæ. The epithelium is present in layers and is characterized by the varied form and size of its elements, which, in the deep layers, are round and small; in the middle layers, cylindrical or spherical with processes; and at the surface rounded, many-cornered or, frequently flattened and larger.

The *Bladder* possesses the same membranes as the ureters. The muscular layer is, very often, quite thick; the individual fibres, however, are distributed so irregularly that their schematic course cannot be described. Usually there is found, internally a net of circular bundles, that cross each other at acute angles, in this way forming meshes that lie transversely. These circular fibres are thickest at the opening of the bladder and here form the sphincters of the bladder. Upon these circular bundles follow longitudinal fibres, which in their turn have a very inconstant distribution. The trigonum consists simply of a thickening of the connective tissue layer, extending from the opening of the ureter to the caput gallinaginis. The mucous membrane (except at the trigonum) has a thick sub-mucous layer; this is rich in blood vessels and nerves (especially at the neck and fundus of the bladder).

In the neck of the bladder and towards the fundus are found simple racemose glands, which have cylindrical epithelium and mucous contents.

In the bladder is found epithelium that is arranged in several layers and, like that of the ureter differs in the different layers. Innermost are found cells, that have a more flattened form, but varying very much in respect to form and size. The middle layer, is usually composed of young, conical cells, presenting their apices toward the cavity of the bladder, whose processes can be frequently traced into the deeper layer. The outer layer is composed of ovoid cells irregular, and frequently where in contact with the middle layer, drawn out.

The superior and inferior vesical arteries, branches of the hypogastric, supply the bladder with blood; these enter the wall of the bladder at the fundus, pass through the muscular

coat, obliquely, giving off branches to the same; and then divide into capillaries in the connective tissue under the epithelium. In the connective tissue at the fundus, where they are not numerous, the nerve fibres can still be distinguished as possessing white substance of Schwann. Their terminal branches are not known. The vessels and nerves of the ureter are analogous to those of the bladder.

The *Male Uretha* has a corpus cavernosum whose structure is like that of the penis, fibrous membrane and meshes, only much more delicate; and a glandular organ—the prostate gland, which forms its support. Under the mucous membrane, throughout its whole extent and below it, there is a well developed connective tissue layer, rich in elastic fibres; there are to be found also organic muscular fibres, arranged both longitudinally and transversely.

The epithelium of the male urethra is cylindrical and arranged in layers; with the exception of the exterior part of the fossa navicularis where papillæ, and flat epithelium are already to be found. The cells of the accessory glands, those of the prostate, Cowper's and Littré's glands, and of the vesicula prostatica are conical and can hardly be distinguished from those of the urethra.

The *Female Uretha* has no corpus cavernosum; the mucous membrane is rich in vascular supply, and has flat epithelium in layers. In addition there are very few glands of Littré to be found in it.

CHAPTER II.

Excretion of the Urine.

The function of the kidney is to excrete the urine; that of the bladder and ureters, on the other hand, to collect, retain and carry it off. A theory which is entirely satisfactory, and explains all facts, concerning the excretion of urine does not, as yet, exist.

Bowman, relying upon the anatomical structure of the kidney, thinks that the epithelial cells are secretory organs, and that water only, is excreted by the tufts, which washes the constituents of urine out of the epithelial cells. Ludwig bases his theory, on the one hand, upon the different amount of blood pressure in the various blood vessels of the kidney; on the other hand, upon the different capacity that substances possess of passing through animal membranes. He assumes, that the pressure upon the glomeruli is greater than in the capillaries surrounding the uriniferous tubules. As a result, an abundant transudation of water, and salts in solution (serum of blood, little albumen and fat) must take place from the blood into the Malpighian capsule. In this way there is to be found in the uriniferous tubules, a very dilute urine and in the capillaries surrounding the tubule, blood that is very much concentrated.

These two fluids, differing so widely in density, and separated from each other by animal membrane, produce active currents of diffusion, as a result of which, water is added to

the concentrated blood, on the one side; and on the other, products of retrograde metamorphosis (urea) and salts are added to the dilute urine in the uriniferous tubules. In this way the watery urine becomes more concentrated, richer in urea and salts; becomes urine. The absence of albumen is to be explained, in that this substance does not easily pass through animal membranes, and then only as a result of increased pressure (the walls of the blood vessels and tubules are animal membrane): accompanying pathological conditions, with increased pressure in the glomeruli (stasis in the veins of the kidney) albumen is always found in the urine, but under normal pressure this is never the case. Although this theory explains many physiological and pathological facts, yet it does not explain how an alkaline serum of the blood produces an acid urine. According to this mechanical theory of Ludwig the excretion of urine is a process of filtration taking place in the glomerulus and a process of diffusion throughout the course of the tubules; the epithelial cells lining the tubules are not taken into consideration at all.

According to Goll and Max Hermann, the difference in pressure between the contents of the vessels and urinary tubules, is the principal force that causes the transmission of the constituents of the urine from the blood to the tubules. According to this, when pressure is increased in the renal artery, the quantity of urine also increases; but when the pressure in the artery is diminished, or when, pressure in the ureters is increased, blood pressure remaining normal in the ureter, the excretion diminishes and, can even stop entirely, long before the pressure in the ureters equals that in the renal artery.

Ustimowitsch and Grützner, have elaborated this theory,

in so far, that they showed, by means of experiments on dogs, that only the local pressure in the glomeruli, not the general blood pressure must be taken into consideration.

Upon section of the medulla in the dog, and electric irritation of the same, producing increased blood pressure, excretion of urine ceased entirely, because, the smaller vessels of the kidney contracted. If the nerves on one side going to the kidney were divided, there would follow, upon this side, a profuse flow of urine, whilst, upon the other. no urine would flow from the ureter. By means of division of the nerves going to the kidneys, its smallest arteries become dilated and relaxed, in this way increasing pressure in the smaller vessels and stimulating the flow of urine.

In addition, Ustimowitsch demonstrated that an increase in excretion of urine can take place even when the general blood pressure is diminished. If the splanchnic nerve be divided, which contains the vasomotoric tracts for the kidney, the pressure in the aorta is diminished—at the same time, however, dilatation of the smaller arteries in the kidney ensues so that an increase in excretion can be verified.

Heidenhein and Wittich support the views of Bowman, in that they show that in their experiments with indigo-sulphate of sodium, urate of sodium and carminate of ammonium these substances are secreted principally by the epithelium of the tortuous tubules.

According to the experiments of K. Müller, the quantity of urine is increased by the action of cold upon the skin; warm baths, on the other hand, or varnishing the surface of the body, the latter producing dilation of the blood vessels in the skin, cause a diminution in the urine.

An increase in the circulation of the skin, then increases, a diminution of the same diminishes the excretion of urine.

According to Wendt, the addition of intra-abdominal pressure impedes the excretion of urine. Possibly pressure in the veins increases, which, as is known (Ludwig) diminishes the quantity of urine.

Maly, Donath, and Posch state that by osmosis, a solution that is made up of several different salts (for instance mono and disodic phosphate) which together possess a neutral or even alkaline reaction, may result in one having an acid reaction. This is exceedingly important because the necessity of ascribing to the epithelial cells the property of causing the formation of acid is entirely unnecessary.

Notwithstanding all the explanations, all hypotheses are not completely satisfactory when all physiological and chemical processes in excretion of urine are taken into consideration We must, therefore, still look upon this process as a combination of secretion and filtration.

CHAPTER III.

THE URINE.

A.—In General.

Urine is the secretion of the kidney, and in the normal condition represents a solution of those substances that pertain to retrograde metamorphosis. It is a solution of urea and common salt, to which are added, in small quantities, other organic and inorganic constitutents of the blood, also, certain substances introduced into the system which are excreted either in their unchanged condition or after having undergone a chemical decomposition.

In the normal condition the urine contains organic constituents (urea, uric acid, creatinine, hippuric acid, xanthine, lactic acid, grape sugar, etc., Brücke); inorganic constituents (chloride of sodium, phosphate of sodium, calcium and magnesium, sulphates of the alkalis, salts of ammonium and iron, in combination with the coloring matter and gases, carbonic oxide, nitrogen and oxygen).

In pathological urine there can be detected, in addition to these normal substances, albumen, grape sugar, inosit, constituents of bile, fats, sulphide of hydrogen, blood coloring matter, uorērythrine (Heller), leucine and tyrosine, calcic carbonate and oxalate, carbonate of ammonium, cystine, pus, blood, epithelial structures, spermatozoa, fungi and infusoria.

Before considering the symptomatological value of urine, we must look at its properties (as far as they interest us) and the most valuable methods for its examination.

B.—Physical Properties.

I. Quantity.

The quantity of urine that is voided by a healthy man that eats and drinks moderately, in twenty-four hours, varies from 1.400–1.600 c. c.; average, 1.500 c. c.

The greatest quantity is secreted during the afternoon, the smallest during the night; the mean occurs in the morning, and at this time the urine represents, in every respect, an average, being least influenced by meals.

By means of the introduction of fluid into the system the quantity of urine can be enormously increased (urina potus); an increase, less marked, can be noticed during very cold or moist weather (less perspiration). During rest or great perspiration and profuse diarrhœa the quantity is diminished.

II. Specific Gravity.

The *Specific Gravity* of a normal urine of 1.500 c. c. quantity is from 1.015 to 1.021. If the quantity increases or diminishes the specific gravity changes in inverse ratio. In pathological cases the specific gravity varies from 1.003 to 1.040. Those cases are of special importance, in which with small volume there is low specific gravity, or with great volume high specific gravity. A high specific gravity is found frequently in diabetes mellitus, in the beginning of acute diseases and during the administration of salts. Urine of great quantity, having a specific gravity of between 1.003 and 1.040 is always very suspicious as indicating diabetes mellitus. A low specific gravity is observed in hydruria, urina spastica and urina potus.

Specific gravity can be accurately determined either by means of the picnometer or the scales of Westphal. For practical purposes, however, small areometers (called urinometers) are employed.

If the specific gravity is to be determined by means of the urinometer, a suitable vessel is filled four-fifths full, all air-bubbles are removed with filtering paper, and the urinometer then introduced in that, it is allowed to slide between the index and middle finger of the right hand. The urinometer must not be allowed to touch the walls of the vessel. Bring the eye on the same plane with the surface of the fluid, and read from that division of the scale that corresponds with the surface of the urine (not with that surface that is drawn up on the scale by means of attraction). [NOTE.—A simple rule is to read from the lowest level of the fluid; in this way both attraction of the walls of the vessel, and also of the stem of the urinometer, are disregarded]. Then the urinometer is immersed into the fluid and again read.

In taking specific gravity with the urinometer, the temperature must be between 12–17° C., otherwise a great error can be made.

If the quantity of urine for observation be very small, it is to be diluted with two, three or four times its volume of water, the urinometer is then introduced, and the result is multiplied by the diluted volumes. Thus, if one volume of urine has been diluted with three volumes of water, and the areometer marks 1.008, the real specific gravity is obtained from this apparent specific gravity by multiplying the last two figures of 1.008 by $1+3=4$:

$$1.008 \times 4 = 1.032.$$

The same quantity of solids that was dissolved in one volume is now dissolved in four; the specific gravity after dilution is, therefore, only one-fourth of the real, or the real specific gravity is four times that of the dilute.

III. Solids.

The quantity of solids secreted in the urine in twenty-four hours varies between 60 and 70 grammes. If a greater amount, than 200.00 gr. is found, we have to deal with DIABETES. If, on the other hand, the quantity being nearly normal, we find only 20.00 grammes, we have HYDRURIA. In order to determine, approximately, the quantity of solids present in 24 hours, either Trapp's (2) or Haeser's (2.33) coëfficient can be employed. (For accurate determination see Chapter V.) First, the specific gravity of the urine is found. If the last two figures are multiplied by the coëfficient, the answer will be the quantity of solid constituents found in 1000 c. c. (in grammes.) If the quantity of urine is known, we can easily determine from this how much there is found in 24 hours. For instance, we have a urine of 1500 c. c. in quantity during 24 hours, its specific gravity is 1.020; in order to find the amount of solids in 1000 c. c. the last two figures, 20, are multiplied by Haeser's coëfficient 2.33:

$$20 \times 2.33 = 46.60.$$

This product represents the amount of solids, in grammes, in 1,000 c. c. of urine; from this we can readily establish the proportion:

$$1{,}000 : 46.60 :: 1500 : x,$$

and in solving it find the quantity in 24 hours. In this instance, x=69.90—nearly the normal quantity.

In the following, the quantity of solids in 24 hours of different urine will be given:

Ex. I.—Quantity, 4,000, c. c.
Sp. gr. 1.007.
07×2.33=16.31.

1,000 c. c. urine, therefore, contain 16.31 gr. solids—4,000 c. c.=65.24 gr. From this we see that the quantity of solids is normal, that the water alone is increased.

Ex. II.—Quantity, 6,000 c. c.
Sp. gr. 1.013.
13×2.33=30.29.

In 1,000 c. c. urine we have 30.29 gr. solids in 6,000 c. c.:

1,000 : 6,000 : : 30.29 : x
x=181.74 gr.

In this urine the solids in 24 hours are more than double the normal quantity, we having here a case corresponding to diabetes.

Ex. III.—Quantity, 2,000 c. c.
Sp. gr. 1.005.
05×2.32=11.65 gr.

1,000 c. c. contain 11.65—2,000=23.30 gr. The solid constituents are very much diminished—an hydruria.

The differential diagnosis between diabetes, insipidus and hydruria on the one hand, and urina potus on the other; as also between oligenia and normal urine, can be made simply by taking the solid constituents of the 24 hours into consideration.

Other important deductions can be drawn from the quantity of solids and the specific gravity, the observer being guided by the individual case under observation. Thus, a

disease of the kidney has been demonstrated; the quantity of urine being normal or diminished, and the specific gravity very low, the deduction can be drawn that as urea represents nearly one-half the solids; this substance is not excreted in sufficient quantity, uræmia may be imminent, etc.

As the ratio of the solids in solution is not constant, the calculation from the specific gravity cannot be accurate. An error of 6% can be made (in abnormal urine even more), *i. e.* having computed in 1,000 parts 50 gr., of solids, and finding only 47 or 53 gr., on the next day we cannot say that the solids have increased or diminished.

In judging the changes in the body by the specific gravity, we must, in addition, take into consideration whether or not the usual amount of food is taken up, or (as in acute diseases) whether the patient abstains from food. In the latter instance, an average of 30.00 gr. must be taken, so that a patient passing 40.00 gr., having pneumonia and abstaining from food, really passes more than the normal quantity—an increase that takes place at the cost of the body.

IV. Consistency.

The consistency of normal urine is that of a thin fluid that can be easily separated into drops. Under pathological conditions the urine becomes thick. When a great amount of pus is present in alkaline urine, the urine can be drawn out like the contents of a cyst containing paralbumine. Diluted with water and precipitated with acetic acid, a dense cloudiness arises, which is an alkaline albuminate, formed by the action of the alkaline urine on pus.

In Isle de France, it is stated that urine is observed that coagulates in the vessel like lymph, and contains fibrine

(fibrinuria). In our zone this form of urine is exceedingly rare. In several cases of papillary tumors of the bladder we have observed temporary fibrinuria.

The urine that was fluid at the time it was voided, reddish-yellow and containing very little blood, in a few minutes was changed to a trembling, gelatinous mass, that could no longer be poured from the vessel that contained it.

Upon shaking normal urine a foam is formed which disappears in a very short time when the vessel is put down; if the urine contains sugar or albumen the foam will remain for some time. (Bile also gives to urine a certain amount of tenacity, so that bubbles are retained upon the surface for some time.)

V. Color.

The normal color of urine of 1.020 sp. gr. and 1500 c. c quantity in 24 hours, is wine-yellow. In concentrated urine it varies from dark wine-yellow to that of amber; in diluted, from pale wine-yellow to straw-colored. The urine passed in the morning; or when people have perspired, always has a dark, and urina potus a light color. In addition, in pathological conditions, the urine undergoes much greater changes, for which, very commonly, abnormal coloring matter must be looked upon as the cause.

Urine can be divided into the following varieties, in respect to color:

1. *Nearly Colorless.*—Especially in neuroses do we meet with a "urina spastica," which can hardly be distinguished from water. In other varieties of hydruria and diabetes, the coloring may be very faint, although the yellow is unmistakable. A change, however, can set in in the course of a few hours, so that then a darker urine is passed.

Light urine arises from the presence of the normal quantity of coloring matter in much water (urina potus, urina spastica) or normal amount of water and diminished coloring matter (as in the granular kidney); in most cases both factors are present.

2. *Highly Colored.*—Dark yellow, somewhat reddish, to red. This color is not only produced by concentration, but frequently by the presence of uroërythrine. It is met with in fever, in the stages of increase and acme.

3. *Blood Red to Garnet* is always produced by the presence of some foreign coloring matter. Numerous substances from the vegetable kingdom, when excreted by the kidneys, impart to alkaline urine a red color. The same occurs when blood is found in the urine

4. *Dark Brown to Black* is caused by the presence of methæmoglobine in diseases of the kidney, especially hemorrhages, by the presence of biliary coloring matter in the urine (icteric urine-jaundice) and by coloring matter that is not definitely known to us, as in long-continued attacks of intermittent fever.

Sometimes in melanotic cancers, after the urine has been allowed to stand for some time, it becomes black. As this form of coloring matter has been found without the presence of a cancer and *vice versa*, not much symptomatic reliance can be placed upon its presence or absence. After the external use of carbolic acid (according to Lister's method) very dark urine is also observed, but this is not constant.

Occasionally in the urine of children, a brownish discoloration going from the surface to the bottom is observed, due to the presence of pyrocatechine. In lepra we see the dark red urine changed to a dark brown, as the fatal end approaches (urorubrohematine).

5. *Green*, of a dirty shade, is produced in jaundice, by the presence of biliverdine, and is of the same importance as brown, icteric urine.

6. *Bluish*, that produces a dark blue film and a similar precipitate of indican. The urine always is alkaline—most frequently met with in cholera and typhus.

VI. Transparency and Fluorescence.

Normal urine is always clear and transparent, and only when it has stood for a long time can we distinguish a small cloudiness of mucus (nubecula). With the microscope, there are found in this, epethelial cells, flat and round.

The nubecula, in females, is usually more abundant and more epithelium is found in it, especially in layers, coming from the genitals. Pathologically the urine becomes cloudy from all those substances that are found in the sediment.

If we want to detect the chemical nature of the turbidity, the following method is employed: A test-tube is filled one-third full with the urine that we wish to examine, and carefully heated over a lamp.

(*a*) If the cloudiness disappears entirely, urates which are beginning to be precipitated are suspended.

(*b*) If the cloudiness does not disappear, but, rather, seems to increase, it may depend on carbonate of calcium, the earthy phosphates, or albuminous cellular elements (pus, blood). In order to differentiate, a few drops of acetic acid are added. If the urine clears up, the earthy phosphates have caused the turbidity; if this is not the case, or if the turbidity increases, suspended pus or blood can in most cases be considered the cause.

(*c*) If the urine does not undergo any change when heated, and a slight increase in cloudiness, only, be detected, a greater amount of mucus and bacteria, than normal, can be deduced.

Normal urine sometimes is markedly fluorescent; as yet we are unable to state the substances that produce it. Alkaline urine, by reflected light, appears greenish; by transmitted, yellowish red. Some urine shows the spectrum of urobiline.

VII. Odor.

The odor of fresh human urine is faintly aromatic. The substances causing this are unknown. If the urine has undergone alkaline fermentation, a distinct ammoniacal odor is perceptible. In destructive processes in the bladder, a peculiar, fetid, sometimes fecal smell is present. Upon the introduction of certain articles of food, or the taking of certain drugs, the odor of the urine is changed in a marked manner; for instance, after eating asparagus, cauliflower, etc. After turpentine, the odor is like that of violets. The odoriferous principles of cubebs, saffron, etc., can also be detected in the urine.

VIII. Reaction.

Normal urine has an acid reaction; this depends principally upon the acid phosphate of the alkalies.

It may be produced, also, by free organic acids (lactic ?) At all events the rôle that is played by these acids in producing the reaction is secondary. If to a fluid, containing free acid, a solution of sodic hyposulphite be added, it becomes turbid on account of the precipitation of sulphur.

If this experiment be tried with urine, even after 24 hours a very slight, sometimes no, turbidity sets in; therefore, (even if we do not consider this test as absolute), the amount of free acid in the urine cannot be very great. Sometimes, after a meal, alkaline urine is voided; this, however, disappears in a short time, and is of no clinical importance.

Great acidity of the urine is important to the physician, in that it may favor the development of sediments or concretions, and may give rise to irritation of the kidneys and the urinary passages (Vogel).

Acid reaction may be changed to neutral or even alkaline. The use of the carbonates of the alkalies and earths, or organic salts (acetates, pomates, tartrates,) which change to carbonates in the organism, may cause the urine to become alkaline. The urine may also be alkaline from carbonate of ammonia, that has been formed by urea taking up water.

At first, the quantity of ammonium-corbonate is only sufficient to neutralize the urine; therefore, the neutral reaction is of the same value as the alkaline.

An urine of strong alkaline reaction always points to disease of the bladder, provided excretion of alkalies by the urine has been excluded.

The test is, usually, very delicate bluish violet and faintly red litmus paper.

We must discriminate between the change to the alkaline taking place before or after the urine leaves the bladder. Furthermore, whether the alkalinity depends upon ammonium carbonate (splitting up of urea), or fixed carbonate (absorption). This can be done by allowing the litmus paper to lie in a warm place until it becomes dry; if ammonium

has produced the change, the red color reappears; if this does not take place, the alkalies present are fixed.

Occasionally urine is observed that turns blue litmus red, and red, blue. This reaction is known as the *amphoteric*, has found no explanation, and has no symptomatic importance.

CHEMICAL COMPOSITION.

(a) NORMAL ORGANIC CONSTITUENTS.

We preface the discussion of the individual substances by a table representing the average quantity excreted. In 24 hours there are voided:

	Grammes.	Per cent.
Solids	60—70	4.3—4.6
Urea	30—40	2.5—3.2
Uric Acid	0.4—0.8	0.03—0.05
Creatinine	0.5—1.0	0.036—0.062
Hippuric Acid	0.3—1.0	0.02—0.06
Chlorides	10—13	0.7—0.8
Earthy Phosphates	0.9—1.3	0.07—0.08
Phosphoric Acid	2.5—3.5	0.19—0.22
Sulphuric Acid	1.5—2.5	0.16—0.17

From this we see that the greatest amounts are represented by urea and the chlorides. From this it is easily understood how, when one of these substances is absent in urine, a decided effect is produced upon specific gravity.

This does not hold good, equally, for the other normal constituents, as they are excreted relatively in very small quantities.

The amount of gases is practically unimportant. Carbonic acid gas is present in greatest amount (60—150 c. c. in 1,000 c. c. urine). Nitrogen is present in very small amount, and of oxygen traces only can be discovered.

I. Urea.

Urea CH_4N_2O, is the most constant constituent and the one that occurs in greatest amount. In 24 hours a healthy adult will excrete between thirty and forty grammes of urea.

Animal diet produces greater quantities of urea than mixed, and the latter more than vegetable food, exclusively. In inanition the quantity falls to twenty, even fifteen grammes. The latter figures must be taken into consideration if we wish to form an idea of the changes in the economy of patients put upon absolute diet.

Urea is obtained from the urine in the simplest manner, as follows: After precipitating the inorganic salts with the barium solution used in the volumetric urea test, evaporate to dryness, extract with alcohol, filter, then evaporate the alcohol; finally recrystallize the crystals with absolute alcohol. Another method consists in concentrating urine to the consistency of a thin syrup, then adding pure nitric acid (cold), as a result of which nitrate of urea is precipitated. These crystals are decomposed with carbonate of barium, and then drying, the urea is extracted by alcohol. Synthetically urea can be made from ammonium cyanate; 80 parts of ferro-cyanide of potassium are melted with 30 parts of carbonate of potassium in a crucible. By means of 150 parts of litharge the cyanide of potassium that has been formed (CNK) is changed to the cyanate CNOK. This is then poured upon an iron plate. After it has cooled it is dissolved in a solution of 80 parts of sulphate of ammonium ($(NH_4)_2SO_4$) in 500 parts of water; a double decomposition takes place, producing $CN, O.H_4N$ cyanate of ammonium and K_2SO_4 (potassic sulphate), then filter and dry. Whilst evaporating, the transposition of atoms takes place, so that from the cyanate of ammonium we obtain urea—as follows:

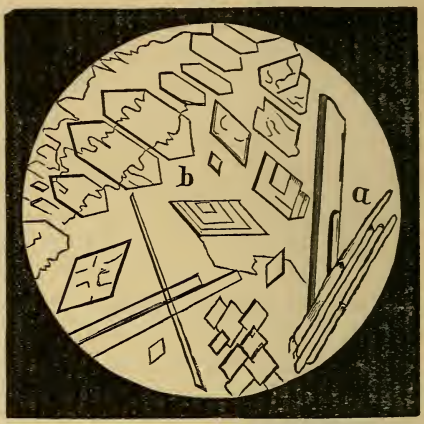
$$O\overset{CN}{\underset{NH_4}{}} \quad = \quad CO\overset{NH_2}{\underset{NH_2}{}}$$

(Cyanate of ammonium.) (Urea.)

The dried mass is extracted with alcohol, and allowed to crystallize.

Urea crystallizes in the form of glistening, white needles (under the microscope); when viewed with the naked eye, in long, transparent quadrilateral prisms, whose ends are terminated by one or two slanting planes. It is easily soluble in water and alcohol, but insoluble in ether. Heated, moderately, on platinum, it melts and develops ammonia. Mixed with putrescent urine, or the secretion from cystitis, it is separated in the opposite way from its formation. It splits up into 1 molecule of carbonic acid gas and 2 molecules of ammonia, taking up 1 molecule of water ($CH_4N_2O+H_2O=CO_2+2H_3N$).

Fig. 3.



a, Crystals of urea; *b*, crystals of nitrate of urea.

This same decomposition takes place when boiled with strong mineral acids, melted with caustic alkalies, or when heated with caustic barium in a sealed tube. When nitrous acid, hypochlorite or hypobromite of sodium are added, urea is split up into carbonic acid, water and nitrogen.

Urea is carbamide. For details see K. B. Hofman's Zoochemistry—in English—Fowne's Elementary, or Kingzett's Animal Chemistry.

Nitrate of mercury, with solutions of urea, produces a flaky white precipitate, equalling 2, 3, or 4 equivalents of mercury to 1 of urea, according to the concentration of the fluid. With common salt, also, urea enters into combination.

When nitric acid is added to concentrated urine, or to a concentrated solution of urea, beautiful rhombic plates are formed, which may frequently be seen with the naked eye.

If one has only a drop of fluid which must be tested for urea, this is put upon a slide; a drop of nitric acid is added; this is gently heated over a spirit lamp, then put aside to crystallize. Under the microscope there are observed, either single rhombic or hexagonal plates, or these are seen in great number, more or less developed, lying upon each other like shingles, and in rows, generally, intersecting each other at right angles. The acute angle of the rhombus is 82°. This test is most frequently resorted to on account of the facility with which it is carried out, and also on account of the characteristic form of the crystal of nitrate of urea.

In albuminuria the nitrate of urea takes another form, that of brush-shape needles. (Hoffman. l. c.)

A concentrated solution of urea, decomposed by oxalic acid produces crystals that look like those of nitrate of urea; but as this form does not appear so regularly as the former, this reaction is looked upon more as corroborating and verifying, having been preceded by the nitric acid test.

These reactions can all be carried out with concentrated urine, but when albumen is present, this must first be gotten rid of, by means of coagulation.

If the question comes up whether a fluid is urine, the first thing to be decided would be the determination of the presence of urea and uric acid. If a few drops only were presented, the micro-chemical reaction for urea would be decisive. We must not forget, however, that some transudations contain urea.

As urea, of all the constituents of urine, is present in

greatest quantity, we can deduct from the specific gravity, approximately, the quantity of urea, provided no sugar and no great amount of albumen can be detected, and provided the chlorides be present in normal quantity. This being the case, and a urine whose specific gravity is between 1020 and 1024, we can state that such an urine contains a normal percentage of urea, *i. e.*, between 2 and 2.5 %. If, under the same conditions, we find increased or diminished specific gravity, we can state that the percentage of urea is, correspondingly, increased or diminished. If the specific gravity is 1014 the urine contains about 1 % urea; if 1028–1030, it contains 3 % urea.

If the chlorides are present only in small quantity or can not be detected at all, as occasionally happens in acute febrile diseases, even with normal specific gravity, then the percentage of urea is increased; for the 16 grammes of chlorides that are present in normal urine, and which is the second greatest factor in influencing specific gravity (always excluding sugar and albumen), are absent in this case, therefore the specific gravity of 1020 must be produced by the urea; for all the remaining constituents of urine, uric acid, creatinine, the phosphates and sulphates, if they were increased to even double their normal quantity, could have very little influence upon the specific gravity.

If albumen be present in moderate quantity (0.2%), which can be detected by means of the nitric acid test, producing a translucent layer of precipitate, it has very little influence upon the specific gravity, and can be neglected entirely in the approximation of urea. But if albumen be present in greater quantity (1–2 %), then it must be re-

moved by coagulation and the filtered urine must be examined after it has cooled off.

For this purpose it is best to take a given quantity of urine, for instance 50 c. c., heat it in a flask, after having added a few drops of acetic acid, to the boiling point; allow it to cool, then filter and wash the filtering paper with distilled water until the fluid that has been lost by evaporation is made up. Thereupon the specific gravity of this urine that has been deprived of albumen is determined.

Usually urine containing albumen is of itself of a lighter specific gravity than the normal urine on account of the disease of the urine-producing organs preventing the secretion from containing that quantity of excreted matter (especially urea) that is found when the kidney functionates normally. As a result, the specific gravity must become less. The quantity of albumen is rarely sufficiently great to substitute the urea in regard to the specific gravity.

When sugar is present in large quantity, then the per cent. of urea is always diminished, although the entire quantity of urea excreted is always increased. The high specific gravity depends upon the sugar.

Although we have never succeeded in obtaining urea from proteïne, artificially, notwithstanding many statements to the contrary, yet this must be considered as its only source. Urea is not the only, but the most important, measure of tissue change. It owes its origin partly to the retrograde metamorphosis of tissue (including the blood), partly to the decomposition of superfluous nitrogenous food. Whether urea originates in gradual oxidation; whether its molecule is separated from one more complex, by means of fermentation; whether this separation takes place from the albumen-

molecule directly, or from a gradual division of this molecule into smaller ones (intermediate molecules), from which, by oxidation, urea is generated, is, as yet, undecided. It is proven that certain combinations that are found in the body, belonging to the uric acid group (uric acid, allantoïne, creatine, sarcine, xanthine, guanine), and certain derivates of proteïne (glycocoll, leucine, aspartic acid), when introduced in considerable quantities into the body will produce an increase in urea.

An increase of the urea, to such an extent that upon the addition of nitric acid a pulp of nitrate of urea is formed is found:

1. When the diet is principally animal.

2. In acute febrile diseases, until the acme is reached. Urea in this case comes from increased wear of the nitrogenous elements.

3. In diabetes mellitus and insipidus.

Urea is diminished:

1. When the diet is vegetable and in fasting.

2. In chronic diseases where tissue change is impaired (cachexias).

3. In parenchymatous affections of the kidney, accompanied by uræmia, especially before death (7 gr.!)

The percentage of urea is diminished in urina potus, spastica and diabetes, but if the quantity in 24 hours be taken into consideration, it will be found that the urea is usually increased, at least it is present in normal quantity.

II. Uric Acid.

$C_5NH_4O_3$

Uric acid is always found in the urine of carnivora. The healthy adult usually voids from 0.4—0.8 grammes in 24 hours.

It is sparingly soluble in (14,000 parts of cold and 1,800 of warm) water, and entirely insoluble in alcohol and ether. This alone speaks for the fact, that uric acid is not present free in the urine, but nearly all of it in the form of the urates.

In a warm solution of normal alkali phosphate, uric acid is much more soluble than in water, because it withdraws from the phosphate part of its base. In this way, then, is produced an acid alkali phosphate and an alkali urate.

Free uric acid, as well as its salts, always appears colored in the sediment, the intensity depending on the color of the urine.

In order to obtain uric acid from urine, 20 parts of the latter are mixed with 1 part of hydrochloric acid, and the whole allowed to stand for 24 honrs. A crystalline powder or membrane is separated, consisting of uric acid, on the bottom and walls of the vessel, and also on the surface of the fluid.

The primary crystal of uric acid is the whetstone, or, better, a rhombic vertical prism. In this form, and variations we find it; also in native sediments. If uric acid is separated from urine by means of hydrochloric acid, the forms are somewhat changed. They seem coarser and more highly colored. Usually there are found under the microscope double whetstones, in the form of a cross; groups of narrow and long whetstones arranged parallel to each other, or like needles, which resemble, somewhat, a comb, having teeth on both sides. It is rare to find single crystals. If the uric acid that has been precipitated by hydrochloric acid, is separated by filtration, redissolved in potassium or sodium hydrate, and reprecipitated by hydrochloric acid, the result will be a much whiter deposit. Repeating the process, frequently, will finally produce snowy white crystals, even from human urine. Uric acid can also be puri-

fied by means of dissolving in sulphuric acid and then precipitating by adding a great quantity of water.

In fresh urine, uric acid or the urates ought never to be found; if this occurs frequently, our attention must be drawn to the formation of calculi.

In the formation of gravel and calculi it occurs that concrements of uric acid are passed that are too large for microscopic examination, and, therefore, do not permit of an accurate diagnosis regarding their structure. In these cases the chemical test, murexide, will give us positive results.

To make this test the concrement is pulverized in a small mortar, put into a porcelain evaporating dish, and then a few drops of nitric acid and a small quantity of water are added. This is heated until the uric acid has dissolved, and then the fluids are driven off. Whilst evaporating, if uric acid be present, we notice on the walls of the vessel intense red deposits that disappear as soon as we approach them with the lamp. When the solution has been nearly evaporated to dryness, and a drop of aqua ammonia is added, the whole contents of the dish appear of a beautiful purple (murexide-purpurate of ammonium); then add a drop of a solution of hydrated potassium, and the solution appears violet. This reaction depends upon a change in the uric acid to alloxan and alloxantine, which by the ammonium are converted into murexide.

Instead of using the test, the concrement may be dissolved in potassium hydrate, precipitated by hydrochloric acid and examined under the microscope, the crystals being characteristic for uric acid.

If only small quantities of suspected fluid are at our disposal, they are put into a watch glass, together with a

linen thread, 6-8 drops of glacial acetic acid are added; the whole is allowed to stand for 24 hours at 15°C.

Adding to an alkaline solution of uric acid a diluted solution of cupric sulphate will produce a white precipitate of cuprous urate; if an excess of sulphate of copper is added and then boiled, the red cuprous oxide will be precipitated. The oxygen from the cupric oxide is used for oxidation of the uric acid (we therefore find in the solution urea, allantoine and oxalic acid). This alkaline solution of uric acid will also reduce nitrate of silver. If the two are mixed, in small quantities, upon the filter, there is found a black (if there be 1-1000 uric acid) or, (if 1-500,000 be present) a brownish yellow spot.

By means of ozone, in the presence of an alkali, uric acid is converted into urea, ammonia, oxalic acid and carbonic acid; when the alkali is absent, into urea, carbonic acid and allantoine.

Uric acid is a bibasic acid, and, as a result, two series of salts are formed, neutral and acid.

The neutral salts are more readily soluble in water than the acid salts. Acid urate of soda requires 124 parts of boiling and 1150 parts of cold water to dissolve it. Therefore, if we find urates in the sediment, we know that they are acid salts. On the other hand, if we find urates in solution, especially after the urine has acquired the temperature of the room, we can assume that they are, principally, neutral. This view is supported by the fact that if an urine corresponding to the preceding is decomposed by a strong acid, muriatic or nitric, the whole urine, at first, becomes cloudy. If this cloudiness is examined under the microscope, we see that it is produced by amorphous points, which

are acid urate of sodium. After having stood for some time, the milky cloudiness disappears, and in its stead appears a distinct crystalline deposit of free uric acid. This phenomenon can only be explained by assuming that in the clear urine neutral urates were held in solution, from which, by the addition of acids, some of the base was deprived producing the less soluble acid urates. The acid continuing to act, all the base is taken from the urate, leaving free uric acid.

In the reaction for albumen, when the nitric acid is poured under the urine, it is an established fact that frequently a layer is produced which, by the inexperienced, might be taken for the albumen precipitate. This, however, consists simply of amorphous acid urates, that are changed to uric acid on standing.

The acid urates of sodium and ammonium will find consideration under the heading of sediments. The causes for the increase or diminution of uric acid have, as yet, not found a satisfactory explanation.

Uric acid is considered as a preliminary step toward the formation of urea, although it is not at all probable that all the urea of the body is developed in this manner. From this the increase of uric acid was explained in all those conditions in which oxidation of the nitrogenous excretions is insufficient, either from the presence of too little oxygen or from the increased formation of uric acid, which is too great for the normal quantity of oxygen to dispose of. Many facts, however, do not harmonize with this explanation.

Uric acid, as derivative of proteïne compounds, has the same importance for the economy as urea. Usually, there-

fore, we find an increase of uric acid where urea is excreted in greater quantity.

We find an increase of uric acid:

1. In high living, either animal or vegetable diet, with little exercise in the open air.

2. In acute febrile diseases, where nitrogenous compounds are decomposed.

3. In diseases of the lungs and heart, accompanied by insufficiency of respiration.

4. In all those cases in which the diaphragm is hindered from functionating properly; in large tumors of the abdomen, ascites, etc.

5. In leucæmia, either on account of increased production of uric acid by the diseased spleen, or on account of diminished oxidation by the blood, poor in red corpuscles.

6. In the so-called uric acid diathesis.

A diminution is usually found in chronic diseases of the kidney, diabetes mellitus (occasionally), urina spastica, hydruria and arthritis.

In order to determine, approximately, the quantity of uric acid in urine, the following may be used: Normal urine of 1020–1024 sp. gr. neither precipitates, uric acid or urates, at the ordinary temperature, nor can we detect a precipitate upon using the nitric acid test.

If concentration increases, there will be observed in the sediment a small quantity of free uric acid, and the nitric acid test will reveal a narrow layer. In these cases, however, the specific gravity is already increased; therefore, urea, and with it uric acid, are present in greater quantity. The quantity being normal, and we find much brick-dust sediment, and, in addition, urates in solution, or a consider-

able sediment of uric acid, the uric acid is increased. But if the quantity is diminished, this conclusion can not be drawn. In this case there may not be sufficient fluid present to dissolve the water at the ordinary temperature.

For ordinary purposes it is safe to consider uric acid as diminished where urea is. All that has been stated refers to the quantity in percentage. If we wish to have an idea concerning the whole quantity, we must, naturally, take the quantity of urine passed in 24 hours into consideration. It is best to compare with normal urine. The average quantity is 1500 c. c. We must therefore add enough water to make up these 1500 c. c. in 24 hours. If we take the quantity in 24 hours as 1000 c. c., we must add 500 c. c., or, to 10 c. c. of urine 5 c. c. of water. Two test tubes of equal diameter are selected; into one is put 15 c. c. of normal urine; into the other 10 c. c. of the concentrated urine, and to both are added 10 drops of muriatic acid, and then allowed to stand for 24 hours. From the precipitate we can easily determine whether the uric acid is increased or diminished in the urine that is compared with the standard. If the quantity is greater than 1500 c. c., the corresponding dilution of the normal urine must be had recourse to.

III. Coloring Matter.

In normal urine there occurs urine indican and a pigment, urobiline. Besides these well known bodies, there are found several other pigments that, however, have not been thoroughly studied.

(a) Urobiline.

Urobiline is a brown, resinous mass, readily soluble in water, but more readily in alcohol, ether and chloroform.

Concentrated solutions are brown, varying from a yellow to a pink. They have no reaction with litmus, by reflected light show a beautiful green fluorescence, and with the spectroscope possess a dark band of absorption between the Frauenhofer lines *b* and *F*. The fluorescence and spectroscopic appearance become more distinct upon the addition of ammonia and a trace of chloride of calcium. Upon the addition of hydrochloric acid, however, the fluorescence disappears, and the absorption band approaches *F*, becomes fainter and has less marked outlines. If ammonia is added to the acid solution, its brown or red color is changed to a light yellow, approaching a green. Alkaline solutions show the same absorption band, and, at the same place as neutral solutions.

In order to obtain urobiline, it is advisable to take dark fever urine. It is made strongly alkaline by ammonia. filtered, and then chloride of zinc is added until no precipitate is produced. This is washed upon the filter, first with cold, then with warm water, until nitrate of silver no longer produces turbidity in the water used for washing. Then it is boiled with alcohol, dried at a moderate heat, the powder dissolved in ammonia and precipitated with lead acetate. The precipitate is then washed a little with water, decomposed with a moderate quantity of alcohol, containing sulphuric acid, and filtered. To the filtrate an equal quantity of chloroform is added, shaken, in order to remove the sulphuric acid, adding fresh water until this shows traces of color. Upon evaporating the chloroform, the urobiline remains in the form of a resinous mass.

According to the researches of Maly, urobiline is a result of the reduction of bilirubine. As Hoppe-Seyler has succeeded in producing a compound identical with urobiline, by means of acting on blood-coloring matter with hydrochloric acids and tin, and as, on the other hand, the injection of sub-

stances that destroy the blood corpuscles increases the formation of biliary coloring matter, we can hardly doubt that urobiline is the direct or indirect result of the reduction of haemoglobine, and therefore its increase is of interest to the physician. It is found in acute febrile diseases, and points to an increased waste of red blood corpuscles.

Urine which, without any further preparation, shows a greenish fluorescence upon the addition of ammonia and chloride of zinc and the characteristic absorption line, can be put down as rich in urobiline.

Scherer's urohaematine, Heller's urophaeine, Thudichum's urochrome, etc., are bodies for whose purity we have no guarantee; indeed, for urochrome and urohaematine Maly has shown that both contain much urobiline.

(B) Urine–Indican.

Since the time of Heller, it is known that an addition of hydrochloric acid to urine will produce a peach-blossom red, violet or deep blue discoloration. The red he attributed to urrhodine, the blue to uroglaucine, and the coloring matter, from which both arise, and which he conceived to be yellow, he called uroxanthine. Uroglaucine was also found in urine spontaneously putrid, and has been identified with the indigo of plants. Uroxanthine was therefore considered the same as indican, the mother substance of indigo-white, which is found in many plants. Recent investigations have shown that these two substances are not identical. We will therefore call these bodies urine-indican.

This substance can be obtained pure by means of precipitating with acetate of lead, decomposing with ammonia; this precipitate, suspended in alcohol, is subjected to a current of sulphuretted hy-

drogen gas, then filtered from the lead sulphide, evaporated with gentle heat, finally in vacuo over sulphuric acid. More complicated methods are known. For particulars, see Hoppe-Seyler, Chemische Analyse, p. 191.

Urine-indican is not a glucoside, because, upon splitting it up no sugar is found; it is a bi-sulpho acid on account of the treatment with hydrochloric acids giving large quantities of free sulphuric acid. In the uncombined condition, these acid-ethers are unstable, and putridity, as well as the action of mineral acids, decompose them. Simultaneous, in both instances, there is an oxidation, so that the formation of indigo does not depend solely upon a splitting up. The one product is indigo; a second is a red body, whose sublimate condenses to fine red needles, which might be identical with Heller's urrhodine. Upon the quantity of these two products depends the color which is produced upon the addition of hydrochloric acid to urine.

When concentrated sulphuric acid is allowed to drop into urine from some height, the mixture is usually colored more or less dark red. This seems to depend upon various products (probably the splitting up of urine coloring matter). In the presence of sugar, albumen and constituents of the bile, undoubtedly all participate in the splitting up, so that the mixture may become opaque and brownish black (Heller's urophæine test). As this mixture generates a considerable amount of heat, many substances, such as iodine, the odoriferous oil of cubebs, of sassafras, etc., escape, and are detected by the smell. In parenchymatous purulent processes in the bladder, an exceedingly offensive and penetrating odor is generated.

The oldest test for indican is the uroxanthine test of Heller.

1. This is carried out in the following manner: There is poured into a beaker 3–4 c. c. of pure hydrochloric acid,

and into this are dropped from 10–20 drops of urine, stirring the mixture with a glass rod. Under normal conditions, there is present only sufficient indican to give to the mixture a light yellowish-red tint. If the acid, however, becomes violet or blue, then the quantity of indican is greater than normal. The more indican there is present, the more rapidly does this change take place, and sometimes 1 or 2 drops of urine are sufficient to give to 4 c. c. of urine a blue tint. If after 1 or 2 minutes no violet is perceived, then indican is not increased, even if the mixture should turn dark reddish-brown after standing for from 10–20 minutes.

In the urine of jaundice, it is necessary to precipitate the biliary coloring-matter with acetate of lead, and filter before performing the test.

The color in this test, unfortunately, is of little value, as it does not only represent the quantity, but also the varied capability, of decomposition of indican; how inconstant this is, is proven by the fact that urine-indican produces, at one time more indigo blue, at another more indigo red. Above all, it must be observed that albumen, with hydrochloric acid, especially when the action has gone on for some time or it has been heated, shows a violet color. Notwithstanding this, the dark blue color may be looked upon as a sign of increase in indican.

2. 10 c. c. of urine are mixed with equal quantities of hydrochloric acid, then drop either a saturated solution of chloride of lime, or simply chlorine water, into the mixture, and observe the color (Jaffé's test).

3. Heat about 5 c. c. of urine, moderately, with double the quantity of nitric acid, then shake with chloroform, which takes up the indican. Finally examine the chloroform extract with the spectroscope (Stokvis' test).

If indol is introduced into the system, indican is very much increased; the same occurs if the small intestine is ligated. The pancreas digestion produces, in its last stage, indol; by tying the intestine this is increased, absorbed and finally produces an increase in the urine-indican. The albumen of food, then, is a source of indican. In the ordinary putrefaction of albumen indol is generated. On the other hand, it is becoming more probable that a part of the albumen in the body, on account of a fermentative process is divided up as it would be by putrefaction outside of the body. The albumen of the tissues, then, is the other source of indol, and therefore of indican. In this way may be explained how, in fasting, indican does not entirely disappear from the urine, being formed at the cost of the disintegrating tissues.

Indican is increased; in meat diet, in Addison's disease, in cholera, in cancer of the liver; it is enormously increased in all diseases that produce a closure of the small intestine (incarceration, invagination, etc.); not so much in obstruction of the large intestine; ordinary constipation. It is very much increased in cancer of the stomach and peritonitis. In disease of the kidney, with the exception of the granular kidney, indican is not much increased. In general, chronic consumptive and inanition-processes increase it rather than acute diseases. Fever does not cause the same increase in indican that it does in urobiline.

Increase of urine-indican in lesions of the central and peripheral nervous system has only been determined by means of the reaction for uroxanthine, and therefore awaits further, more accurate investigation to make this result positive.

IV.—Other Normal Organic Constituents.

The remaining organic constituents, up to the present, possess very little value in aiding diagnosis; we therefore will mention them but briefly:

Kreatinine—the strongest base in the body—is passed in the same quantity as uric acid. The average quantity in 24 hours is between 0.6—1.3 grammes. In vegetable diet the quantity is smaller than in animal diet. It has been found increased in pneumonia, intermittens and typhus; diminished in inanition, advanced disease of the kidney.

Hippuric Acid is found principally in the urine of herbivora. In human urine it is found in very small quantities. The average quantity is between 0.5 and 1.0 grammes in 24 hours. After eating certain kinds of fruit (Reine-claudes, etc.), after the administration of benzoic acid, hippuric acid is increased. This is also the case in febrile diseases and in diabetes; it is diminished when exclusive meat diet is used. If the quantity is increased very much, hydrochloric acid will cause a precipitate of hippuric acid just as it would of uric acid.

Xanthine and the phenol-producing, disulphonic acid, are found in very small quantity in the urine. The former can only be obtained from several hundred liters of urine, in sufficient quantity for qualitative tests. The presence of phenol-forming substances is detected by the phenyl reaction of the urine when this has been previously acidulated with a strong mineral acid. If tartaric acid, however, is used, the destillate of normal urine shows no phenol reaction, proving that phenol (carbolic acid) exists in urine only in a combined state.

Oxaluric Acid is found in very small quantity. It is the result of the indirect oxidation of uric acid.

Oxalic Acid is found in the sediment in the form of its calcium salt.

Concerning the existence of *Sugar* in normal urine, the authorities are divided. At all events, there is found in normal urine a substance which, in common with the urates, will reduce copper sulphate in alkaline solutions.

In normal urine the existence of *Lactic Acid* has not been positively decided upon. In pathological urine two kinds of lactic acid are found; fermentation lactic acid, occurring in fermenting urine of diabetes; sarcolactic acid after phosphorous poisoning, in acute yellow atrophy of the liver, in malacosteon and trichinosis.

B.—Normal Inorganic Constituents.

1—.Chlorides.

In human urine we find the chlorides to consist nearly exclusively of the chloride of sodium and very little chloride of potassium. The average quantity found in the urine of a healthy man for 24 hours is from 10 to 16 grammes (6–10 gr. chlorine). After urea, chloride of sodium is the principal constituent of urine—indeed, corresponding with this fact the urine possesses a salty taste. If a drop of urine is evaporated on a slide, and put under the microscope, there will be found, besides the rhombic plates of urea; chloride of sodium in flat octohedra or incompletely developed crystals of the tessular system.

It is frequently important for the physician to find out in an easy and quick manner whether the chlorides are increased or not. This can be done in the following way:

If a solution of common salt is decomposed by nitrate of silver, a white precipitate of chloride of silver is produced:

$$NaCl + AgNO_3 = NaNO_3 + AgCl.$$

But if we have a solution which also contains phosphates, as urine, we must first acidulate with a little nitric acid before making this test, so as to prevent the phosphoric acid from precipitating with the silver, thus increasing the latter. An unimportant inaccuracy is produced by the simultaneous

precipitation of uric acid. The nitric acid prevents the formation of phosphate of silver, but not of the insoluble chloride. If, for this test, a solution of nitrate of silver of constant strength (1 in 8) is taken, we find that if single drops of this solution are added to ½—1% solution of common salt (as urine), they will fall to the bottom of the vessel in the form of cheesy masses, that are not subdivided upon shaking and never produce a cloudiness. If we have a very dilute solution, 1-10% and under, no masses are formed, but the whole fluid becomes equally milky and turbid.

This method can be utilized for the examination of urine in the following way: A wine-glass is taken, filled half full with urine, acidulated with nitric acid, and then 1 or 2 drops of the silver solution are added. If the drops come down as cheesy globules, the chlorides are not diminished; if a milkiness is produced, they are very much diminished, and if this is wanting, they are entirely absent.

The test for albumen can be made to serve for the test for salt. Stir the nitric acid with the urine, and then add the nitrate of silver. If much albumen is present, the coagulum must be removed by filtration before performing the test for the chlorides.

The chlorides are diminished:

1. When the body is at rest (the night urine has a small quantity of chlorides).

2. In all acute febrile diseases, especially if combined with serous exudations or watery passages. The quantity of chlorides is in direct ratio with the quantity of urine, and in indirect with the specific gravity and quantity of urea, until the acme is reached. As a rule, the kidney excretes only the excess of chlorides. In inflammatory processes

common salt frequently collects in the exudations (pleuritis). On the whole, it can be said of the chlorides, in connection with acute processes, that an increased diminution of the chlorides indicates an increase of the disease, and *vice versa*.

In pneumonia, for instance, the chlorides can be entirely absent without our being able to account for this by a diminished introduction into the system. In typhus and meningitis they are diminished, but not absent. Absence of chlorides always indicates a grave affection.

3. In chronic diseases, with diminished digestive powers, or dropsy.

Increase of the chlorides is observed:

1. When much salt is introduced.

2. When much physical or mental labor is performed.

3. During paroxysms of fever, either before or after. Throughout the 24 hours this is compensated for, so that the whole quantity is normal, or even sub-normal.

4. In diabetes insipidus.

5. In dropsy, as soon as diuresis has been established, so that the pent-up chlorides suddenly find an escape.

2.—Phosphates.

The whole amount of phosphoric acid is between 2.3 and 3.8 grammes; in healthy men the average is 3.5 grammes. The diurnal variations can be very great. The quantity rises after the meal until evening (maximum), and falls during the night until the next morning (minimum).

We find an increase of phosphoric acid in urine:

1. After the introduction of phosphorus, phosphoric acid or the soluble phosphates into the organism.

2. When the diet is principally animal, and especially when food is taken that contains more or less prepared phosphoric acid as brain.

3. In all acute febrile diseases (not always).

A diminution is found in all urine of low specific gravity: urina potus, urina spastica, etc., in kidney and in heart disease, with diminished urine; in serious disturbances of digestion, and in chronic brain troubles (except epilepsy).

Phosphoric acid PO_4H_3 is a tribasic acid, *i. e.*, the three atoms of hydrogen can be displaced by metals.

In urine this acid is partially bound by the earthy, partially by the alkaline bases (earthy and alkaline phosphates).

(*d*) The earthy phosphates, *i. e*,, of calcium and magnesium are found, normally, in very small quantity (0.9–1.3 grammes in 24 hours). Magnesium phosphate is present in about double the quantity of calcium phosphate. In acid urine we find these salts in solution; in alkaline urine, however, they are found in the sediment.

Phosphoric acid forms, with calcium, three salts:

The neutral:

$$\left.\begin{matrix} PO\left\{\begin{matrix} O \\ O \\ O \end{matrix}\right. \\ PO\left\{\begin{matrix} O \\ O \\ O \end{matrix}\right. \end{matrix}\right\} \begin{matrix} Ca \\ Ca \end{matrix} = (PO_4)_2Ca_3$$

The single acid:

$$PO\left\{\begin{matrix} OH \\ O \\ O \end{matrix}\right\} Ca + 2H_2O = PO_4HCa + 2H_2O$$

The double acid:

$$\left.\begin{matrix} PO\left\{\begin{matrix} OH \\ OH \\ O \end{matrix}\right. \\ PO\left\{\begin{matrix} O \\ OH \\ OH \end{matrix}\right. \end{matrix}\right\} Ca + H_2O = (PO_4H_2)_2Ca + H_2O$$

The last combination is found dissolved in urine. A double magnesium-phosphate is not known. The single-acid is said to be held in solution in urine by free acid (?)

The reaction for the soluble earthy phosphates is performed by alkalies (sodium, potassium, or ammonium).

In calcium phosphate, acid is withdrawn thus:

$$3[(PO_4H_2)_2Ca]+12KOH=(PO_4)_2Ca_3+4PO_4K_3+12H_2O.$$

With magnesium-phosphate, on the other hand, ammonia magnesic-phosphate is formed if ammonium is used:

$$PO_4HMg+NH_3+6H_2O=PO_4Mg(NH_4)+6H_2O.$$

The crystalline form will be described in connection with the sediments.

In order to test for the earthly phosphates, fill a test-tube one-third full with clear urine, add a few drops of caustic potassium or ammonia, and heat until the earthy phosphates precipitate in flakes; put the test-tube on a stand for 10–15 minutes, so that the precipitate deposits, and then judge of the quantity. If we have used a test-tube about 16 c. long and 2 c. in diameter, a layer of 1 c. in depth will represent the norm; if the layer is 2–3 c. high, the earthy phosphates are increased; if only a few flakes are present, they are diminished.

In normal urine they form a white precipitate; if the urine contains abnormal coloring matter, this determines the color of the precipitate; blood-coloring matter renders them blood-red or dichroic; vegetable coloring matter of rhubarb or senna, etc., pink or blood-red; biliary coloring matter, yellowish-brown and uroerythine gray.

Diseases of bone, malacosteon, rhachitis, etc., extensive periostitis, chronic arthro-rheumatic processes; the introduc-

tion of mineral waters rich in calcium, medicines and exclusive meat diet (not constant), produce an increase of earthy phosphates.

A diminution is observed in diseases of the kidneys.

In alkaline urine the earthy phosphates are found in the sediment.

(*b*) Alkali phosphates are represented (principally) by the acid phosphate of sodium and of potassium (traces).

The tribasic phosphoric acid forms three alkali salts, depending on 1, 2 or 3 atoms of hydrogen being displaced by the metal:

PO_4H_2Na	PO_4HNa_2	PO_4Na_3
(Double-acid, Sodium Phosphate).	(Single-acid, Sodium Phosphate).	(Neutral, Sodium Phosphate).

Only the first has an acid reaction, and its presence produces the acid reaction of urine. The other two have an alkaline reaction. All are readily soluble in water (in contradistinction with the earthy phosphates), even in alkaline water.

Of the entire phosphoric acid found in urine two-thirds are bound to the alkalies.

The reaction is best performed with the magnesia fluid (see Chap. IV., No. 10). If we want to examine for all of the phosphoric acid in urine, we add to 10 c. c. urine 3 c. c. of the magnesia fluid. There is produced a precipitate which is made up principally of ammonia-magnesic phosphate, with which amorphous calcium-phosphate is mixed. If the entire fluid becomes milky, the alkaline phosphates are present in normal quantity. If the precipitate becomes so dense as to give to the fluid the consistency of cream, then the phosphates are increased. If the fluid is simply turbid and very transparent, then there is a diminution.

This is a reaction for the entire phosphoric acid, but as the earthy phosphates are present only in such small quantities, they need either not be taken into consideration, or, with a little practice, one learns to subtract the quantity found by means of the test for the earthy phosphates from the result obtained by this test.

If the earthy phosphates are present in very great quantity, they must be precipitated by ammonia, the urine filtered, and to this the magnesia fluid must be added.

4. Sulphates.

The sulphates found in urine are the neutral sulphates of sodium and potassium.

The sodium salt, as is the rule everywhere, is found in greater quantity than the potassium salt. The quantity of sulphuric acid passed by the healty adult in 24 hours, is between 1.5 and 2.5 grammes—average 2.0 grammes.

The reaction for sulphuric acid is performed in a manner similar to that for phosphoric acid. Into a test-tube is put 10 c. c. of urine, a few drops of hydrochloric acid are added in order to prevent barium-phosphate from being precipitated, then add one-third the quantity (3–4 c. c.) of a solution of chloride of barium. The reaction takes place according to the following formula.

$$BaCl_2 + Na_2SO_4 = 2NaCl + BaSO_4,$$

Sulphate of barium being the desired precipitate. The solution of chloride of barium can be previously acidulated with hydrochloric acid (Chap. IV., No. 7), this precluding the necessity of acidulating the urine.

If there is produced an opaque, milky turbidity, then the sulphates are present in normal quantity; if the consistency

is changed to that of the cream, then they are increased, and if there is produced only a translucent turbidity, then the sulphates are diminished.

A rough quantitative test has been described by J. Vogel. It depends upon the above reaction and is performed by taking 100 c. c. of the urine (2.00 grammes of sulphuric acid being voided in 24 hours with a quantity of 2,000 c. c.) and adding sufficient chloride of barium solution to satisfy one-half the sulphuric acid contained in the 100 c. c. of urine—*i. e.*, 0.05 grammes. If upon the further addition of the test solution no precipitate is formed, then the sulphates are diminished. If a precipitate is produced, then add the same quantity of the test solution that was originally employed, and again test. No precipitate being produced, the sulphates are normal. If a precipitate is produced upon the further addition of the fluid, the sulphates are increased.

An increase of sulphuric acid or the sulphates is observed:

1. After the introduction of sulphuric acid, its soluble salts, of sulphur combinations, or of sulphur itself, into the organism.

2. In exclusive meat diet, the sulphur of the albumen being oxidized to H_2SO_4.

3. In acute febrile diseases, accompanied by free excretion of urea. Increase in the sulphuric acid, in this case, must be referred to an increased waste of those constituents of the body that contain sulphur. The highest degree is noticed in meningitis, encephalitis, rheumatism, and affections of the muscular system.

A decrease in the sulphates occurs in exclusive vegetable diet, in the beginning of typhus and (in percentage) in all those urines that show diminished specific gravity.

Other inorganic substances that have been found in urine are; ammonia, iron and silicic acid. Traces of all only are found but for the first, Duchek claims that as fevers increase, so the ammonia increases, to diminish in reconvalescence.

C.—Abnormal Constituents.

1. Albumen.

Normal urine ought never to contain albumen. In pathological conditions, however, notably in diseases of the kidney, albumen is frequently found in great quantity.

After the taking of much albumen of eggs, Cl. Bernard, Becquerel and others have observed albumen in otherwise perfectly healthy urine. Serum albumen (up to 0.1 %) may be present in the urine of perfectly healthy persons. We have reported several cases (Wiener Med. Presse, 1870,) and also Vogel. The cause for this is unknown. The urine was somewhat concentrated, very acid and contained more urea and uric acid than normal. In the sediment we sometimes found nothing, sometimes crystals of uric acid or oxalate of lime. It is probable that this albuminuria, periodic and presenting variable quantities of albumen, was due to the chemical composition of the urine. It might, also, be attributed to certain abnormal nervous conditions of the kidney. At all events, these cases are of such rare occurrence that the presence of albumen must be considered as abnormal.

Why albumen is not found in the healthy condition is best explained by the mechanical theory of Ludwig.

Graham divides all bodies into crystalloids and colloids: the first, those that diffuse readily through animal membranes; the second, those that diffuse with difficulty or not at all and do not crystallize. This division, applied to albumen, will show that serum albumen is a colloid, for it does not crystallize, nor does it pass through animal membranes unless increased pressure is applied. The crystalloids passing so readily through membranes and the colloids with such diffi-

culty, it is natural to assume that the molecule of albumen must be larger than that of any crystallizable salt. The probability for this increases when we consider the facility with which foam is produced in albumen solutions, and also its complicated chemical structure. The latter finds expression in the formula $C_{216}H_{169}N_{27}S_3O_{68}$.

According to Ludwig we have in the glomerulus, a process of transudation, while throughout the course of the tubules we have one of diffusion. The two fluids, blood and the water of urine, are always found separated by animal membrane. These septa have the property of allowing the crystalloid substances of the blood (salts, urea, etc.,) to pass through readily, but not the albuminoids, under the conditions of pressure in the kidneys, therefore we cannot expect to find albumen in normal urine.

If we find albumen, then the blood pressure in the vessels of the kidney is usually increased (passive hyperaemia, valvular heart disease, amyloid degeneration of the vessels, etc.) or the membrane, in some place, has become pervious (parenchymatous nephritis, Bright's disease).

Albumen is found in urine most frequently as serum albumen and paraglobuline. If other fluids that contain albumen (blood, pus, exudations, etc.,) are present in the urine we will find that form of albumen that is characteristic of these. Fibrine is found in copious hemorrhages and croupous affections of the urinary apparatus.

True fibrinuria, a so-called coagulable urine, that is said to occur frequently in Isle de France, is, with us, a very rare occurrence. We observed this, temporarily only, in three cases of papillomatous tumors of the bladder. But we not infrequently find urine having the consistency of honey

or syrup, depending upon pus dissolved in alkalies, not upon fibrine. This form of urine becomes thin upon the addition of water, and acetic acid produces a white precipitate of alkali-albuminate. This being produced by the action of ammonium carbonate on the serum-albumen of pus.

For albumen there are many characteristic reactions; for the urine, however, two especially are of value,—the concentrated nitric acid test and boiling.

1. In carrying out the nitric acid test about ten c. c. of of urine are put into a glass (best a wine glass or a sherry glass), and under this is poured pure, colorless, concentrated, (not fuming) nitric acid. The reagent is poured under the urine by means of holding the glass containing the nitric acid at an angle with the one containing the urine and allowing the acid to flow gently along the side of the latter. At the place where the acid and urine touch there appears, when albumen is present, a band-like zone, having both upper and lower boundary-line sharply defined. This can only be mistaken for resins (copaivic acid) or the urates; the latter, when present in great quantity, also precipitating upon the addition of nitric acid. But this layer does not appear where urine and acid touch, but higher up; neither is its upper margin sharply defined, resembling more a cloud of smoke, slightly curly in the middle.

If albumen and the urates are present at the same time, two white layers, superimposed, will be obtained. The lower one being albumen, the upper the urates. Both are separated from each other by a layer of clear urine.

The precipitate produced by resins is dissolved by the addition of a few drops of alcohol.

If this test is performed with normal urine, there will be

observed between urine and nitric acid a brown ring of coloring matter which, in a few minutes, increases in intensity. We now comprehend how in fever urine, rich in coloring matter, which at the same time may contain albumen, the ring of albumen will be, not snowy white, but, more or less, brownish. If much indican is present the albumen frequently appears pink or violet; in the presence of blood-coloring matter, red and with biliary coloring matter, not decomposed, of a green color. If urine is very much concentrated, there will be produced a copious crystalline deposit which, under the microscope, will reveal itself as nitrate of urea. Urine, rich in uric acid might produce free uric acid in the form of yellowish whetstones, which can be readily differentiated from the preceding precipitate by its insolubility in water.

If urine contains much carbonic acid, either on account of its being alkaline and having much carbonate of ammonia, or being neutral or acid, having sodium carbonate or free carbonic acid gas (as is frequently the case in the use of mineral waters), then there will be observed upon the addition of nitric acid an effervescence of the fluid.

If this test does not convince to satisfaction, then the next must decide; indeed, it is always best to perform both tests.

2. The test by boiling is performed in that we take 8–10 c. c. of urine, if it be acid, and boil it in a test tube. It is always safer to add 1–2 drops of acetic acid. A flaky cloudiness indicates albumen. If the urine is neutral, faintly acid or alkaline, a precipitate may show itself on boiling, which, upon the addition of acetic acid, again dissolves. This is not albumen, but the earthy phospates that have been held in solution by carbonic acid gas, which, being driven

out by heat, no longer can dissolve. That which has only been done, as a precaution in acid urine, must always be done in alkaline or neutral urine in order to prevent deception, viz: first acidulate the urine.

By means of this test, albumen is not only simulated, but in alkaline urine it may entirely escape detection. The nitric acid test frequently fails us here, on account of the effervescence produced by the reaction upon the carbonates. If we do not acidulate, the alkali present may be sufficient to change the albumen to alkali-albumen, which does not precipitate upon boiling. If we are not careful, on the other hand, with the addition of acetic acid we may err on the other side, producing acid albumen, which can not be precipitated by boiling. In the presence of very small quantities of albumen, its detection becomes a very difficult matter if the urine is already cloudy or does not come through the filter as clear urine. Alkaline urine is already more or less turbid, contains no earthy phosphates in solution and must always be clarified before proceeding to test for albumen. In order to do this the urine must be boiled with ¼ of its volume of caustic pottash (Chap. IV., No. 5.) and filtered. If the filtered urine is not clear 1–2 drops of the magnesia fluid must be added, the urine again heated and filtered. If this is then carefully acidulated with acetic acid the slightest turbidity of albumen will be detected. This becomes more distinct when ferro-cyanide of potassium is added to the already acidulated urine; there will then be noticed upon the bottom of the vessel white flakes of albumen.

It is advantageous to know other tests.

(*a*) **Acidulate the urine with acetic acid, add an equal volume of a cold saturated solution of sodium sulphate, and boil.**

(*b*) Into filtered urine there is dropped saturated solution of picric acid. If cloudiness is produced, albumen is present (Galippés test). Only the cloudiness that is produced instantly is decisive.

Albumen is found in urine:

1. When the blood-pressure in the Malpighian tuft is greater than normal. This occurs in all anomalies of circulation (valvular lesions of the heart, passive hyperaemia, amyloid and atheromatous processes in the arteries, etc).

2. In all those diseases in which a change in the diffusion-membrane, *i. e.*, the walls of the tubule with its epithelium and its arterioles and capillaries, can be demonstrated (parenchymatous nephritis, Bright's disease, etc.).

3. When there is mixed with the urine, blood, pus or any other fluid containing albumen (false albuminuria).

4. Occasionally in hydraemia (disturbance of nutrition in the capillaries).

It is also thought (Vogel) that albuminuria can arise from the formation in the blood of a peculiar kind of albumen, endowed with different properties of diffusion, being even able to pass through the perfectly intact membrane. We have never been in the position, however, to verify this view.

In true albuminuria it is important to be able to determine the quantity of albumen excreted in 24 hours, for only by means of this can we determine whether or not improvement is taking place. The most accurate quantitative analysis of albumen is made by means of the scales or the polariscope (Chap. V.). These methods, however, are too laborious and consume too much time for the practicing physician, and we therefore desire a method by which we are enabled to state when albumen is present in great (1–2%)

or in small (½%) quantity. This can be accomplished, with a little training, by means of observing the albumen-zone produced in the nitric acid test. If this zone is faint, whitish, not granular, more or less translucent, and only to be distinguished as a sharply-defined band when placed against a dark background, and, above all, is only between 2 and 3 m. m. high, then we know that albumen is present in very small quantity (below ½%, usually 1 part in 1,000). If this zone is between 4–6 m. m. high, white, opaque, perceptible without a dark background, granular, then albumen is present in moderate quantity (¼–½%). But when, upon the addition of nitric acid, the albumen precipitates in flakes or granules, sinks to the bottom in small masses, and when upon stirring this mixture with a glass rod the urine has the appearance and consistency of cream, then the quantity of albumen is very great (1–2% and above).

Similar results can be obtained with the boiling test. Take a test-tube and fill it one-third full with clear, filtered urine (if alkaline, acidulate with acetic acid). A very slight turbidity, which permits the urine to appear translucent after boiling, simply causing opalescence, indicates a small quantity of albumen. If the urine is milky, upon boiling, the albumen separating in fine flakes, and upon settling, we find a layer at the bottom of the test-tube of a finger's height, then albumen is present in moderate quantity. But if the albumen separates in coarse flakes, and not, as before, from the upper surface of the fluid, but where the flame touches the tube; if the urine appears thick, like cream, after boiling, then albumen is present in very great quantity. If we wish to compare the quantities of albumen of one day with that of another, it will be necessary to boil in test-tubes of equal

diameter, taking the same quantity of urine, and then compare the height of the sediments. It is better to use glass tubes of equal diameter, that are closed by means of a cork, wrapped in wax paper. After 24 hours we can measure, with a rule, the depth of the albumen layer

The preceding are short directions for approximate analysis, but they must be frequently exercised, and only he who has made himself perfectly familiar with the appearances can draw reliable conclusions.

What has been said is true for the majority of cases, where the principal quantity of albumen is serum albumen.

At the same time, or independently, we frequently find modifications of albumen, of which the most important is globuline (perhaps myosine).

Peptone is found in every urine containing albumen; in diseases in which there is a very high temperature it is sometimes found, even without the presence of albumen.

In order to detect globuline, we dilute the urine until it has reached a specific gravity of 1002. Then we carefully add very dilute acetic acid (it is soluble in the concentrated acid). There usually appears a cloudiness. In order to precipitate all the globuline, allow a slow current of carbonic acid gas (bubble after bubble) to pass through the urine for 1–2 hours. If allowed to stand for a time, the globuline separates in the form of a white powder. The fluid can then be tested by the other methods for serum albumen. If the sediment is made up of globuline, it must be soluble in a few drops of concentrated solution of common salt.

Globuline is found in considerable quantities in catarrh of the bladder, acute nephritis, and especially in the amyloid kidney, whilst it is said that in chronic Bright's disease it is present in very small quantity, or even entirely absent.

2. Sugar.

$$(C_6H_{12}O_6)+H_2O.$$

The sugar of urine (identical with grape sugar) is, according to Brücke, a normal, constant constituent. But it occurs in such small quantity that, when using Trommer's test, not even a slight yellow precipitate is perceptible. Only a discoloration is observed. In abnormal urine, and especially in diabetes mellitus, we frequently find so great a quantity of sugar that it imparts a sweet taste to the urine, and when clothes are moistened with the latter, after the water has evaporated they look as if they had been dipped into honey.

Sugar of urine crystallises in warty concrements that consist of cauliflower leaflets.

Of the many tests, the following are usually sufficient:

1. *Heller's Test.* Mix, in a test-tube, urine, with one-half its volume of caustic potash, or soda solution (1 to 3), and boil. First the earthy phosphates are precipitated; these can be filtered if they are present in very great quantity; as soon as the fluid is heated it is colored lemon, yellowish-brown or brownish-black, according to the quantity of sugar contained. If to this mixture a few drops of nitric acid are added, the dark color disappears, and an odor of caramel becomes perceptible.

If the urine contains much albumen, it is advisable to remove this first by boiling.

If urine is of high color, which rarely happens in diabetes mellitus, it can be decolorized by means of sugar of lead solution (the sub-acetate precipitates a small quantity of sugar), or by filtering through animal charcoal. The latter must afterward be washed with water, because it will retain much sugar.

If this change in color takes place while the urine is cold, then biliary coloring matter is usually present. This change will even appear when the coloring matter is already decomposed, *i. e.*, when neither Gmelin's nor Heller's tests will indicate its presence. In this case this test, especially when the addition of sulphuric acid produces a very dark color, is a very good one for biliary coloring matter.

According to Bädecker, if urine is mixed with caustic potassa and exposed to the air, there gradually appears a brown discoloration, the urine absorbing much oxygen and containing a body which he called alkaptone. This, like sugar of urine, reduces copper, but not bismuth salts. Probably this body is pyro-catechine.

A beautiful reaction is produced by Mulder's test. Mixing urine with a solution of indig-carmine, first made alkaline with sodium carbonate and boiling, the blue mixture first becomes green, then purple, and finally yellow. Shaking the boiling mixture and exposing to oxygen, it again comes back to the original blue.

2. *Trommer's Test.* As before, mix with the urine caustic potassa or soda solution, and add drop by drop, shaking constantly, a solution of copper sulphate (1 to 10) until a clear, blue fluid is obtained. Then heat over a lamp. If sugar is present, reduction of the oxide of copper takes place in the following manner: First, yellow cuprous hydrate is precipitated; this losing its water, leaves red cuprous oxide. If the test-tube is put aside, and we wait a few minutes, there will be observed a metallic mirror covering the bottom of the tube. Albumen must be removed by coagulation. If this is forgotten, a violet color, upon the addition of the reagents, will be a reminder of its presence. If neither sugar nor albumen is present, then we get a turbid grayish green fluid, but no reduction of the oxide.

Large quantities of creatinine, peptone, etc., can prevent the precipitation of the cuprous oxide.

3. *Böttger's Test.* Mix the urine with the alkali, as above, then add as much bismuth—a mixture of basic bismuth nitrate $(BiO)NO_3+BiO,OH$ with bismuth nitrate $(BiO)NO_3+H_2O$—as will cover the end of a knife-blade, and then boil. After a time, a mirror of bismuth appears on the test-tube. If small quantities of sugar are present, then the bismuth is only colored gray, because only a part of it is reduced—the reaction may even be covered over by the excess of bismuth.

If albumen is present, this must be removed, otherwise bismuth-sulphide may be produced, which may be mistaken for an oxide of bismuth. In order to be certain, it is well to add to a portion of urine that has been made alkaline, acetate of lead; if a black precipitate is formed, it is conclusive evidence of the presence of a sulphur compound.

Brücke recommends, in order to remove all disturbing substances, Frohn's reagent (1.5 grammes precipitated, unwashed bismuth nitrate are heated to the boiling point with 20 grammes of water, then 7.0 grammes of iodide of potassium, and finally 20 drops of hydrochloric acid added). A modification has been proposed by Maschke, he using a solution of tungstate of soda.

Heller's test is the simplest and the best, and has the advantage that with it, one skilled in its use, can tell the approximate quantity of sugar present. Second comes Böttger's test, for when no albumen is present, no other substance except sugar will reduce the bismuth. Trommer's test is least reliable, for many other substances, when present in the urine in large quantities, will reduce the copper salt: uric acid, the urates and hippuric acid. Many specimens of urine from patients with acute febrile diseases, where the urates are present in great quantity, are diagnosti-

cated as containing sugar, especially if reliance is placed on the yellow discoloration, not waiting for the precipitate of cuprous oxide. For all cases, the most reliable tests are by fermentation and with the polariscope, both, however, too laborious for the practioner.

If we have demonstrated the presence of sugar, it is of equal importance to determine the quantity present and the amount passed in 24 hours. The exact quantitative tests will be discussed hereafter—they alone are reliable. Approximately this has been determined by the specific gravity; the higher this is, the more sugar is supposed to be present. This, however, is only true for a pure solution of sugar, not for so complex a fluid as urine, and Bence Jones has shown that the method can not even be utilized for rough estimates.

The second method is that of Vogel, and depends upon the intensity of the color produced with the potassa test. It is very useful for the practitioner. If we make solutions of grape sugar of different strength and test them, in test-tubes of equal diameters, a scale can be easily constructed which will suffice for ordinary rough estimates. Mix two parts of the solution with one of liquor potassa, and boil. A 1% solution will give a canary-yellow; a 2%, a dark amber; a 5%, a dark rum, and a 10% solution will become dark brown and opaque, while all other solutions are more or less transparent. Taken in connection with the specific gravity, this test is very useful, as diabetic urine is usually of a very pale color.

Sugar only occurs, in large quantities, in one form of disease: glycosuria.

Temporarily it is found in certain injuries of the brain. In very small quantities it is said to appear in the urine of acute febrile

diseases, spontaneous gangrene, pneumonia, typhus, rheumatism, acute encephalitis, in diseases of the nervous system, especially of the cord, in cachexias, and similar processes; also, after the introduction of turpentine, nitro-benzole, nitrite of amyl, etc.

Neukomm and Vogel, exceptionally, have found inosite, both alone and with grape sugar. It is also to be found in Bright's disease.

Some patients suffering with diabetes have a breath that smells of chloroform. The urine, odorless immediately upon being passed, after a short time also begins to smell of the same substance. Upon the addition of chloride of iron, it usually turns reddish-brown. In the distillate of such urine is found both acetone and alcohol, the result of the splitting up of ethyl-diacetic acid.

$$C_6H_{10}O_3 + 2H_2O = C_3H_6O + C_2H_6O + CO_2 + H_2O,$$

(Ethyl-diacetic acid.) (Acetone.) (Alcohol.)

In women, 24-48 hours after ablactation and during nursing (when the milk for any reason is not withdrawn sufficiently), there appears in the urine sugar of milk.

III. LEUCINE AND TYROSINE.

$C_6H_{13}NO_2$ and $C_9H_{11}NO_3$.

Leucine and tyrosine result from the decomposition of albumen and its nearest derivatives. They are found in great quantities in certain glandular organs of the body, when these are subjected to definite pathological changes; in the liver, the pancreas, the spleen, etc. In the urine they have been found only in acute yellow atrophy of the liver, in several cases of phosphorous poisoning, and, in small quanties, in typhus and variola.

If these substances are present in large quantity (usually the case in acute yellow atrophy of the liver), their detection is very simple. Either we find the crystalline tyrosine in the urine, or it, with the leucine, separates, when the urine is concentrated in a

water bath. Occasionally these bodies occur in so great quantity that they partially take the place of urea. They can be recognised by their characteristic microscopic forms. (Fig. 4. *a*, Leucine. *b*, Tyrosine.) If they are not very abundant, and do not appear upon concentrating the urine, a large quantity of urine must be taken, precipitated with basic acetate of lead, filtered, then the excess of lead removed by sulphuretted hydrogen, again filtered, and then the clear fluid evaporated in the water bath down to a small volume. If tyrosine is present, there will be observed a crystalline deposit, after 24 hours. Leucine, which is more soluble, takes a longer time to be deposited. *It is necessary to examine the urine as soon as possible after it has been voided.*

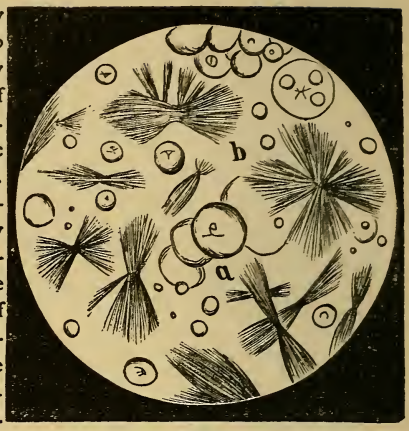


Fig. 4.

When leucine and tyrosine are present in large quantity, great degeneration of the albuminoids is always indicated.

Albumen is nearly constantly found at the same time. Frequently oxymandelic acid $C_8H_8O_4$ (perhaps derived from tyrosine), which, up to the present, has never been observed anywhere else, is found.

IV. Abnormal Coloring Matter.

We must here discriminate between those substances that, being found normally in other fluids of the body, would here be considered abnormal, those that are found only in

the urine, as uroërythrine, and finally those that are entirely accidental, as the coloring matter of plants.

(*a*) Uroerythrine (Harley's Urohaematine).

In all febrile diseases the urine has more or less of a yellowish-red color (urina flammea), and the expert, in most cases, is enabled from the condition of the urine alone to diagnosticate a febrile state. This color, according to Heller, comes from the presence of uroërythrine (besides increase of the normal coloring matter). When such urine has a sediment, this is red or dark red; even the clear urine, when precipitated with lead acetate, will cause a pink or flesh-colored precipitate of lead. Heller calls this red coloring matter, found in solution or in the so-called brick-dust sediment, uroërythrine.

It is said that this coloring matter contains iron; concerning its structure and origin, however, nothing definite is known. It is possible that, in diseases in which there is blood dissolution (typhus, septic fever, etc.), a part of the blood corpuscles in retrograde metamorphosis supply material for the formation of the uroërythrine. The uroërythrine, then, could be taken as measure for the quantity of red blood corpuscles destroyed during fevers.

This coloring matter is either discovered by the presence of a brick-dust sediment, or, when in solution, by the precipitation with lead ascetate above described. Only a small quantity of lead acetate in solution must be added, as it is not advisable to dilute the color in a great precipitate. If the urine contain blood coloring matter, this must be removed. The foam of urine containing much uroërythrine may be yellow, like that of an icteric urine. In the latter, the precipitate with lead is also yellow.

The earthy phosphates, when precipitated with liquor-potassa, appear gray, while in urine containing blood-coloring

matter, they are red or dichroic. The absence of albumen, the color of the earthy phosphates and the red precipitate with lead, are the points of differential diagnosis between uroërythrine and blood-coloring matter.

Uroërythrine is found in all febrile diseases, even in the mildest catarrh; it is found in greatest quantity in pyaemia, diseases of the liver and lead colic.

(β) Coloring Matter of Plants.

Many vegetable substances, especially chrysophanic acid (in rhubarb, senna, etc.) impart to alkaline urine a reddish yellow to deep red color. They can be recognized in that the red alkaline urine, upon the addition of an acid, turns yellow, but after the addition of ammonia again returns to its original red. In the test for the earthy phosphates of an urine containing such coloring matter, these will come down colored blood-red, so that one would be tempted to think of the presence of blood. But the earthy phosphates are never dichroic, and, upon being exposed to the air, turn violet. The differentiation from uroërythrine and blood-coloring matter is accomplished by the absence of a response to the test for blood-coloring matter, the absence of albumen, and by the characteristic changes upon addition of acids and alkalies. It is important that the practitioner be perfectly familiar with these tests, especially in summer when the urine is apt to become alkaline, the blood-red appearance of the urine may be alarming without signification.

(γ) Blood-Coloring Matter.

The occurrence of blood-coloring matter in urine may have a double source. Either it has been excreted by the

kidneys, or the blood-corpuscles that have, originally, been mixed with the urine, have been dissolved. The color of the urine varies in that hæmoglobine or methæmoglobine are present.

In hemorrhages from larger vessels the urine usually contains hæmoglobine. In parenchymatous or capillary hemorrhages the urine usually contains methæmoglobine as well, which imparts to it a brownish-red color. The explanation why hæmoglobine should occur in the one case, and methæmoglobine in the other, is probably to be found in the fact, that in hemorrhages from the capillaries the urine and blood are more intimately and more slowly mixed, and are retained longer at the temperature of the body. The most important factors for the change from hæmoglobine to methæmoglobine are, probably, temperature, the presence of carbonic acid, and the absence of oxygen in the urine.

In order to demonstrate blood-coloring matter in the urine, the hæmine test is advantageous. Precipitate the earthy phosphates in a test tube: these will bring down with them the blood-coloring matter, appearing red. If little blood-coloring matter is present, they are dichroic.

If the urine is alkaline and the test does not bring down the earthy phosphates, because they have already been removed with the sediment, then we can produce a precipitate with 1 or 2 drops of the magnesia solution, which will serve our purpose perfectly.

This precipitate obtained on a filter, then placed upon a slide, dried carefully by means of gentle heat, and we can obtain the hæmine crystals directly from it. To this end place a small quantity of common salt upon the dried earthy phosphates and rub it up well, with a knife. Then blow

the excess of common salt from the slide, place a hair upon the mixture, and upon it a thin cover over the remaining powder, after having added glacial acetic acid; then heat until bubbles begin to form under the covering glass. After cooling, hæmine crystals can be seen with the microscope. The precaution must be taken, in order to avoid further decomposition of the blood-coloring matter, to heat carefully with the liquor potassa and to filter rapidly. Bubbles will also develop under the cover if the slide be allowed to stand, without heating, but these are carbonic acid gas. Allow these to escape, and then heat to the boiling point of the glacial acetic acid. The crystals prepared in this manner frequently appear very small and imperfectly crystallized, but they can be readily distinguished by means of using higher powers.

Another method consists in making the urine alkaline with caustic soda, adding tannic, then acetic acid. The precipitate washed and filtered is then tested for hæmine crystals.

The crystals may also be obtained by coagulating the albumen, collecting the brown coagulum upon a filter, drying and testing with alcohol containing sulphuric acid. Evaporating the alcohol, the residuum is treated in the above manner for Teichmann's hæmine crystals.

If we have a spectroscope at our disposal, a large test tube is filled with the diluted urine, placed between the lamp and the instrument, and we will then observe the characteristic spectrum.

So-called hæmatinuria occurs in diseases of the general system; scorbutus, purpura, scarlatina, etc., after transfusion of blood, after inhalation of arsenetted hydrogen — that dis-

solved blood-coloring matter is found in cases of true hæmatinuria hardly needs to be mentioned.

(δ) Biliary Coloring Matter.

In certain conditions, biliary coloring matter, decomposed or not, can be found mixed with urine. The urine contains biliprasine more frequently than bilirubine; frequently other results of oxydation. If bilirubine is present, unchanged, then the proper tests will give a beautiful and characteristic play of colors; if biliprasine is present, these will produce only a green color; but if the coloring matter has been changed beyond this, the tests are negative.

For the detection of unchanged biliary coloring matter (bilirubine and biliprasine), the following tests may be used:

1. *Gmelin's Test.* Pour under icteric urine concentrated nitric acid containing a small quantity of hyponitric acid. When the two fluids touch, the following colors in the following order will appear: green, blue, violet, red, yellow. Green predominates, while blue is frequently not present. This test can also be performed by mixing urine with diluted nitric acid, and then pouring concentrated sulphuric acid under the mixture.

2. *Heller's Test.* Pour into a small beaker 6 c. c. of pure hydrochloric acid, and then add urine, drop by drop, until the acid becomes faintly colored. Mix, and then pour pure nitric acid under the mixture. Again the play of colors will be observed when the fluids meet. If the fluids be mixed together, this play of colors will take place in the whole mixture. The play of colors can be observed especially well by means of a transmitted light. This test is very delicate, easily executed, and sufficient for nearly all cases.

If we wish to detect small quantities, it is necessary to shake 100 c. c. of urine with 10 c. c. of chloroform in a bottle until the fluid is tinged yellow. Avoid too energetic shaking, as this will so finely subdivide the chloroform that it will no longer unite in large drops. Closing the bottle with the thumb, and lifting the latter, it is easy to allow 1 c. c. of chloroform to drop into a test-tube containing 10 c. c. of pure hydrochloric acid. If, then, a small quantity of nitric acid is added, and the whole shaken, the characteristic play of colors of Gmelin's test will be observed in the drop of chloroform. Because this play of colors takes place slowly, and because acids act very slowly upon this coloring matter dissolved in chloroform, this test is especially valuable for the purpose of demonstration.

In all reactions of biliary coloring matter, the green color is the deciding tint. If this has not been observed, the presence of this coloring matter can not be deduced. Indican, for instance, will also give blue, violet and reddish-yellow, with Heller's test, but the characteristic green is wanting.

In testing for albumen with the nitric acid test, if unchanged biliary coloring matter is present, a green zone will be observed between the urine and the colorless nitric acid. If albumen is present, it is colored green by this test. Urine containing indican, however, may even here simulate biliary coloring matter. A blue layer is produced, which, by reflected light, looks green. In these cases, either perform Heller's test with the chloroform or precipitate the urine with lead acetate, and see if it is possible to detect indican, in quantities, in the filtrate.

3. *Ultzmann's Test.* This strives to bring out the characteristic green color positively and surely. Add to 10 c. c.

urine 3—4 c. c. solution of caustic potassa (1 in 3 of water), shake, and then acidulate with pure hydrochloric acid. The mixture turns emerald green.

If the earthy phosphates are precipitated from urine containing biliary coloring matter, they come down with a brown color.

If the coloring matter is so much changed that the preceding tests are negative, then the following will be of service: Dip a piece of clean, white linen (or filtering paper) into the urine, and allow to dry. The linen will appear brown. A further proof of the presence of biliary coloring matter will be found in a very dark sulphuric acid, reaction. The urine does not become garnet, but black. A similar reaction will only be observed when sugar or blood-coloring matter is present. Both are to be previously excluded.

With liquor-potassa the earthy phosphates are precipitated of a brown color.

Biliary coloring matter is found, in the urine in a variety of pathological changes in the liver, independently of jaundice, so that the latter can frequently be predicted several days before its appearance, by the urine. Furthermore, it is always found in phosphorous poisoning.

V. Biliary Acids.

These are rarely found in urine, and then only in small quantity. In jaundice, although the coloring matter of the bile may be present in great quantity, they are very rarely found. In diseases of the parenchyma of the liver, accompanied by rapid destruction, they are undoubtedly found, but even then in small quantity.

It must be accepted in such cases, that so great a quantity

of biliary acids is produced, that they can not undergo the normal changes in the blood, and are therefore found in the urine.

Sometimes it is possible to demonstrate the biliary acids by means of Strassburger's method. Dissolve a small quantity of cane sugar in the urine that is to be tested, dip filtering paper into it and allow to dry. Going over this with a glass rod, dipped in sulphuric acid, free from nitric acid, will produce a purple-violet stripe (red or reddish-brown is not decisive).

As a rule, however, it is necessary to separate the biliary acids, in a pure state, from a large quantity of urine, and then perform Pettenkofer's test.

The separation is very laborious. Evaporate about 500 c. c. of urine in a water bath to dryness, and extract with ordinary alcohol. This solution, is again evaporated, and the residuum extracted with absolute alcohol. This alcohol is again dissipated and the solid treated with water, the solution precipitated with oxyacetate of lead, avoiding an excess, the precipitate collected, washed, and dried with filtering paper. Thereupon the salts, with lead as base and the biliary acids as acids, are extracted with boiling alcohol; add sodium carbonate, then evaporate again, and finally extract the resulting sodium salt of the biliary acid with absolute alcohol. Now permit the alcohol to evaporate, and, with the concentrated watery solution, perform Pettenkofer's test. This is based upon the fact, that all watery solutions of the biliary acids, when mixed with a few drops of a concentrated solution of cane sugar and concentrated sulphuric acid, care being taken that they are not heated over 70° C. (158° F.), will produce a violet-purple color. It is best, therefore, as soon as the sulphuric acid is added, to put the test tube into cold water, otherwise the sugar will be charred by the sulphuric acid, producing a black color.

A trace can be detected by Neubauer's modification; a few drops of the suspected fluid are evaporated to dryness on a porcelain dish,

upon the water bath. To this there is added a minute drop of a solution of cane sugar, (1,00 gr. sugar in 500 c. c. water) and an equally large drop of concentrated sulphuric acid. Again, heat over the water bath until the violet color begins to appear at the circumference. Then take the dish from the water bath and the reaction will continue to become more marked.

Many other substances, such as amyl alcohol, albumen, oleic acid, give the same reaction, but they can be differentiated by means of the spectroscope.

Besides the substances treated of, there will occur in urine, allantoine, especially after the administration of tannic acid; then lactic, acetic and butyric acids in acid fermentation; benzoic acid in putrid urine, as well as fats and soaps.

VI. Carbonate of Ammonium.

$$CO_3 (NH_4)_2$$

All the carbonate of ammonium that occurs in urine comes from urea. Urea, as has been stated before, is carbamide.

$$CO\begin{cases} NH_2 \\ NH_2 \end{cases}$$

By means of taking up water this is changed to ammonium carbonate.

$$CO\begin{cases} NH_2 \\ NH_2 \end{cases} + 2H_2O = CO\begin{cases} O,NH^4 \\ O,NH^4 \end{cases}$$

This change is the cause of development of ammonium in the decomposition of urine by putridity, which may occur in the bladder. The ferment is a body that adheres to the

mucus of the bladder, and develops best during a catarrh. We therefore find, in nearly all diseases of the bladder the urine of alkaline reaction. The catarrhal secretion of the pelvis of the kidney does not seem to cause alkaline fermentation, certainly only after some time has elapsed; and we therefore find the urine in pyelitis nearly always of an acid reaction. If fresh, normal urine be mixed with the sediment of urine from a pyelitis, and another specimen with that from cystitis, it will be found that the former will require between 12 and 24 hours to show alkalinity, while the latter will become alkaline in a very short time (2 to 3 hours).

Ammonium carbonate is also found in the second stage of processes with exudation, so-called absorption-urine, and is considered, here, a favorable symptom. This substance can be recognized by its odor.

Urine containing it, moreover, is usually alkaline. But the alkaline reaction may depend upon a fixed alkali, as sodium carbonate, which has been taken internally. Whenever there is any doubt about the nature of the alkalinity, the following test can be used:

Put into a small florence flask, 15 to 20 c. c. of the urine then close the flask with a cork, perforated, in order to allow a glass tube, of the thickness of a lead pencil, to pass through. Into this there is put a piece of red litmus paper that has been well moistened. Heat the flask carefully in a water bath; if ammonia is present, it will be carried off with the vapor of water arising from the urine and color the litmus paper blue. Care must be taken not to boil the urine, otherwise urea will be decomposed, giving rise to carbonate of ammonium.

Ammonium carbonate is found:

1. Usually in the various forms of disease of the bladder.
2. In the second stage of acute exudative processes.

According to Heller, this salt is also found in troubles of the spinal cord and grave cases of typhus, even with acid reaction of the urine.

VII. Hyrdogen Sulphide.

SH_2

Occasionally sulphuretted hydrogen is found in urine containing albumen, especially in troubles of the bladder where a great quantity of pus is produced. Here it is formed from the albumen, which decomposes while in the bladder. Although the odor is characteristic, yet it sometimes become necessary to prove its existence by a chemical reaction. In order to do this we use the same method employed for detecting the presence of ammonia, taking instead of the litmus paper a piece of filtering paper that has been dipped either into a lead or silver salt solution. The slightest amount of heat will cause the gas to escape and color the strip of paper brownish-black.

Such urine is easily detected by the fact of its coloring silver catheters black.

Accidental Constituents.

Under this heading we consider those substances that are exceptionally found or introduced into the organism, and then leave it by way of the urine.

Many substances are not changed at all in the system, as; most inorganic combinations, as well as many organic (succinic acid, chloroform, quinia, carbolic acid, etc).

Of the heavy metals the following have been found: antimony, arsenic, copper, zinc, gold, silver, tin, lead, bismuth, and mercury: either as a result of introduction as medicine or on account of constant handling (painters, potters, etc.).

Of the alkali salts nearly all pass into tne urine; the carbonates, ammonium salts, chlorates, borates and silicates of the alkalies, ferro- and ferri-cyanide of potassium, cyanide of potassium, iodide of potassium, etc. Sulphide of potassium is found in the urine as sulphate. On the other hand calcium and magnesium salts are either not found at all, or in very small quantities only.

Mineral acids (sulphuric, nitric, phosphoric, etc.,) are found as the corresponding alkali-salts; only free carbonic acid appears as a simple solution in the urine.

Metallic bases can be detected either by electrolysis or by forming an ash, and then examining in the ordinary way. Arsenic is first precipitated with sulphuretted hydrogen, and then can be easily detected by Marsh's method.

Many combinations, especially the organic, are changed in the organism. The aromatic acids, for instance, are all excreted, as glycocol combinations so; benzoic acid in the urine, as hippuric acid, salicylic acid (for the most part), as salicyluric acid.

Carbonates of the alkalies are found:

1. After the internal administration of the same.
2. After the use of mineral waters.
3. After eating much fruit, because the fruit acids are all converted into carbonic acid in the system.

In these cases the reaction of the urine is alkaline. In order to prove the origin of this alkalinity, evaporate the urine to dryness, then add a little water and test with litmus paper. If we find an alkaline reaction, it is proof positive that there have been permanent alkali salts present in the urine.

Iodine is easily detected by adding to the suspected urine, sulphide of carbon, then fuming nitric acid and shaking (violet discoloration of the sulphide of carbon or chloroform). Starch solution can also be added, and then fuming nitric acid. A bluish discoloration indicates iodine. In Heller's test for albumen, iodine crystals are frequently deposited,

Salicylic acid can be found by means of the violet color produced when cloride of iron is added. A similar reaction sometimes occurs in diabetic urine, even when salicylic acid is absent.

D.—Sediments.

Fermentation of Urine.

Normal urine when voided is clear. After having remained in the vessel for some time, there is formed either at

the bottom of the vessel, or in the lower part of the urine, the so-called nubecula; a cloud of mucus from the bladder, being very well marked when relieved by a black background, or when there is contained in the mucus epithelium, in greater quantity than normal, or bacteria, or, suspended, traces of precipitated urates.

In this condition an healthy urine, placed in a perfectly clean vessel, will keep for a long time; longer when the air is excluded—weeks, even months.

Frequently, however, a change takes place, known as acid fermentation.

In the urine there is found both the acid sodium phosphate and urate of sodium. The phosphate acting upon the urate, by withdrawing some of the base from the urate, changes the latter to an acid salt, which, being insoluble, is precipitated in the form of yellow or reddish powder. This takes place especially at a low temperature. At high temperatures the process of decomposition goes on. From the urate all its base is withdrawn (sodium), and the uric acid being set free, and being comparatively insoluble, comes down in the form of a crystalline brick-dust red, or brownish-red, granular powder adhering to the walls of the vessel, floating on the surface of the fluid, or resting upon the bottom of the vessel. Sometimes these crystals of uric acid are mixed with the amorphous urates that have not as yet been decomposed—brick-dust sediment.

During this process no free acid is produced, as can be proven by the appropriate tests.

In the greater number of instances there is mixed with this sediment oxalate of lime, in small or large crystals. Some of the uric acid is transformed, in the body, into ox-

aluric acid; this, when exposed to the air for some time, changes to oxalic acid, appearing in the sediment as oxalate of lime.

This process, as will be seen, does not deserve the name, fermentation. But in some cases true fermentation, with the formation of acetic acid, takes place.

After this process has come to an end, there begins, sooner or later, another. The urine becomes paler, the crystals of uric acid have disappeared, acid reaction gives way to neutral, which finally changes to alkaline. The urine has an ammoniacal odor, becomes very cloudy, and has a white precipitate, made up of phosphates of the earthy alkalies. Under the microscope, this cloudiness will be seen to be made up not only, of suspended phosphates, but also of innumerable bacteria, at rest and also in motion. This process is actual or alkaline fermentation. The cause is the decomposition of the urea, it being acted upon by a peculiar ferment, discovered by Musculus.

Musculus recommends paper, impregnated with the ferment, as a very delicate test for urea. The thick alkaline urine of cystitis is filtered. The paper used for filtering is washed with distilled water until it no longer reacts alkaline. It is then dried and colored with turmeric. Urea has no reaction upon turmeric, but when the ferment in the paper acts upon urea, this is decomposed and ammonium carbonate thus generated colors the paper brown.

The ammonia may unite with the uric acid to form urate of ammonia. When the formation of ammonia has reached its maximum, a part of it also unites with the phosphate of magnesia to form crystals of the triple phosphate. Phosphate of calcium, which is soluble only in acid solutions, is precipitated, and we have the sediment of alkaline urine,

composed of amorphous masses of calcium phosphate, crystals of triple phosphate, and, in the beginning, of ammonium urate.

Pus, blood or vessels already unclean with urine that has fermented, cause very rapid decomposition of the urine, it not being necessary for the urine to go through the so-called acid fermentation first.

The process is accompanied by bacteria. Various fungi can be observed upon the surface of the urine, especially in warm weather.

Classification of the Sediments.

As long as these formed constituents of urine are mixed with the urine, they cause cloudiness; as soon as they sink to the bottom, a sediment. Precipitation takes place variously; quickly in thin urine containing heavy substances, such as uric acid or urates; slowly in albuminous, dense urine containing light substances, such as epithelium or hyaline casts. The constituents of the sediments are either formed inside or outside of the body. The elements are either organized (occurring both in acid and alkaline urine) or unorganized, partly amorphous, partly crystalline; some found in acid, others in alkaline urine. Accordingly the sediments can be divided as follows:

SEDIMENTS.

I, of acid urine.	II, of alkaline urine.
A.—Non-Organized.	
(*a*) Amorphous.	
1. Urate of sodium and potassium.	1. Calcium phosphate.
2. Fats.	2. Calcium carbonate.

(*b*) CRYSTALLIZED.

1. Uric acid.	1. Urate of ammonium.
2. Oxalate of calcium.	2. Triple phosphate.
3. Cystine.	3. Calcium phosphate.
4. Tyrosine.	4. Magnesium phosphate.

B.—Organized.

1. Mucus and pus corpuscles.
2. Blood corpuscles.
3. Epithelium from the various parts of the urinary apparatus.
4. Casts and coagula of fibrine.
5. Spermatozoa.
6. Cancer tissue.
7. Entozoa.
8. Fungi.

In this order they will receive attention.

Non-Organic Sediments.

1. URATES.

Uric acid is found in urine bound to sodium and potassium and forms salts of variable structure, so that by the withdrawal of base, more acid salts are produced, which become less soluble and, therefore, more ready to precipitate.

Urates are more soluble in warm than in cold water; the neutral salts are more soluble than the acid. From this follows, that when stronger acids are added that displace part of the uric acid from its base, acid (less soluble) salts are produced from the neutral. These, in their turn, precipitate the more rapidly the colder the fluid is, and the smaller the

quantity. The formation of the urates in the sediments is favored, then, by three following conditions:

1. Moderate addition of acid (by means of great acidity the uric acid is precipitated) or the action of acid salts (so-called acid fermentation).

2. Concentration of urine, either by means of the increase of uric acid or by the diminution of water.

3. Cooling of the urine, which takes place naturally only after the urine has been voided or in the cadaver.

The urates of the alkalies are an amorphous powder, which, on account of the coloring matter that comes down with it, appears yellowish, grayish brown, pink or brick-dust red. Under the microscope they appear as small granules, grouped like moss. If mixed with mucus the beginner may mistake the picture for that of a finely granular cast. They can be differentiated, however, by the absence of sharp contours, by the want of plasticity and, above all, by the reaction upon the addition of heat.

The urates disappear when warmed. If any deposit is left, it will be seen to be pure uric acid. Upon the addition of an alkali and heat, even this disappears.

This property of the urates permits a differentiation between pus and the phosphates without the use of the microscope. Phosphates do not occur in urine of a decidedly acid reaction. In urine faintly acid, boiling would increase the deposit, especially if hydrate of potassium or sodium be added.

If the urine contains pus, boiling alone would not make it clearer; on the contrary, on account of the coagulation of the albumen, the deposit would become denser (alkalies, however, would probably prevent this coagulation).

Finally, the murexide test, performed with the dry sediment, or the following beautiful micro-chemical test, would be decisive. Add to the urates that have been placed upon a slide a drop of hydrochloric acid; after a time crystals of uric acid will be observed

There are sometimes observed in urine having undergone acid fermentation, and beginning the alkaline, crystals of uric acid, partially dissolved, but having upon them prismatic crystals of urate of sodium.

2. Urate of Ammonium.

The acid urate of ammonium is the only urate that occurs in alkaline urine and is, therefore, found side by side with the amorphous phosphate of calcium and the triple phosphate.

Urate of ammonium forms brown balls, which are either developed singly, doubly, or in the form of a conglomerate with a kidney-shaped surface. The surface of these bodies is either smooth or it is covered with small spikes, or these processes are long, even divided, and then most frequently curved, producing manifold forms (Fig. 5). These forms are so characteristic that there can be no doubt concerning the nature of these crystals when viewed under the microscope.

Fig. 5.—Urate of Ammonium.

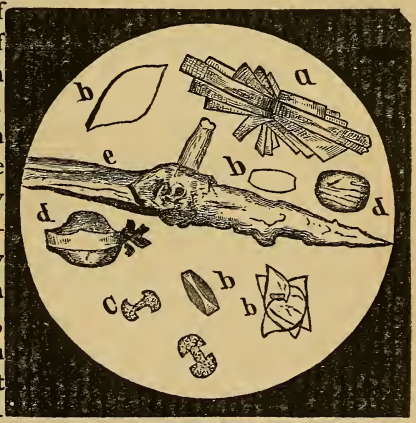
Other tests are the murexide, the formation of uric acid as described above, and, finally, the addition of caustic potassa, producing bubbles of liberated ammonium.

3. Uric Acid.

The occurrence of uric acid is due, partly, to the same causes that have been discussed under the head of urates. Normally the crystals of uric acid are found at the termination of the so-called acid fermentation, in concentrated urine, especially in summer, where high temperature prevents the deposit of urates; then, in pathologically increased formation of uric acid, in which case neither water nor alkalies suffice to keep the acid in solution.

The primary form of uric acid is that of rhombic plates with rounded, blunt corners.

This form is known as the whetstone. The crystals may be very small or developed singly. Sometimes they group about foreign bodies, as threads, hairs, and then form cast-like bodies. At other times the individual crystals are highly developed and collected together, appearing either fan-shaped or like the shingles upon a roof. Besides



Uric Acid.

Fig. 6.

a. Rosette. *b.* Whetstone. *c.* Dumb-bell. *d.* Barrel-shaped. *e.* Lance-shaped.

the whetstone form are found barrel-shaped, and, in other cases, lance-shaped crystals, frequently united to form rosettes. The rough and lance-shape forms are of great practical importance in that they always have some connection with the formation of calculi in the kidney.

They occur only, in very acid urine. If this is counteracted by the internal administration of fixed alkalies, then the form of the crystal changes to the normal, that of the whetstone. These forms are frequently found in the sediment of pyelitis calculosa, and also accompany albuminuria (hyperæmia of the kidneys) and hæmaturia.

Intense desire to pass water, without albuminuria or pyelitis, is occasionally found in those patients whose urine contains these forms.

In ALL cases the uric acid appears colored, faintly yellow, brownish-red or dark brown (on account of coloring matters that are brought down with it).

The crystals are usually so well developed, that they appear as glistening brick-dust red sand upon the bottom of the vessel, and may be diagnosticated with the naked eye.

This sediment is dissolved in caustic alkalies when boiled, being partially changed to urates, partially to lower oxides. Finally, with the sediment, the murexide test is eminently characteristic.

IV. Oxalate of Calcium.

Oxalic acid has great affinity for calcium. As there is calcium in urine, the oxalic acid, formed in the kidney or in the urine, must be found in the latter in the form of oxalate of lime. These crystals, as has been stated, frequently

appear, during acid fermentation, with uric acid. The shape of the oxalate of lime is very characteristic. They are flat octahedra, that refract the light very much, sometimes appearing as small points, sometimes as squares, whose corners are connected by diagonals, so that they appear like envelopes (see Fig. 7). Besides this form, there is also that of the hour-glass (dumb-bell). These crystals easily escape detection by the inexperienced, on account of their low specific gravity, depositing very slowly. In order to detect them, it is necessary to allow the urine to stand for from 12—24 hours.

Fig. 7.
Oxalate of Calcium and Cystine.
a, Cystine ; *b*, Oxalate of Calcium.

The characteristic form of these crystals prevents error in diagnosis. The only crystal that could be mistaken for them is that of the triple phosphate. But, in the first place, the crystals of oxalate of calcium are never as large as those of the triple phosphate—then the latter is always found in neutral or alkaline urine, the former always in acid, and finally acetic acid dissolves the latter and not the former.

V. Cystine.

Cystine forms regular hexagonal plates, differing in size,

arranged either singly, or in such a manner that one or more smaller crystals lie upon a larger one. Sometimes a large crystalline plate shows cleavage—that in its turn corresponds with the outline of a hexagon. Rarely twin-crystals are observed, and small, poorly-developed crystals are collected together in the form of irregular masses. (See Fig. 7, *b*.)

Sometimes the corners of the crystals are rounded off as if they had been melted off. The crystals are always colorless, and can only be mistaken for an exceedingly rare form of colorless uric acid. This could occur, possibly, if the dissolved cystine would be precipitated from the urine by acetic acid, as this would produce a similar, but more irregular, deposit of uric acid in hexagonal plates.

In order to be positive that the crystal under the microscope is cystine, allow a drop of ammonia to flow under the thin cover; the cystine will immediately disappear, while uric acid would remain, unless heated. As soon as the ammonia has evaporated the cystine again crystallizes. This can be hastened when, to the ammoniacal solution there is added a drop of acetic acid. A second test consists in adding to the crystals of cystine a drop of hydrochloric or oxalic acid. Cystine is dissolved, while uric acid remains unchanged. It can not be mistaken for urates, on account of its form; in addition, it is entirely insoluble in warm water.

As cystine is soluble in ammonia, but not in carbonate of ammonia, alkaline fermentation will precipitate it like the earthy phosphates. From these it can be differentiated both by microscopic and chemical tests.

The addition of acetic acid causing the earthy phosphates to dissolve, leaves the cystine unchanged. If, besides this, we boil, the greater part of the sediment may dissolve. The

remnant being placed under the microscope may reveal hexagonal plates, but these must be tested with ammonia and hydrochloric acid in order to separate the cystine from the uric acid that may be present.

If cystine is dissolved in liquor potassa, heated, water and then a solution of nitro-prusside of sodium added, the mixture will turn violet (sulphur reaction).

Urine in which cystine is detected is usually pale; upon decomposition the odor of sulphur, besides that of ammonia, is developed, probably on account of the presence of sulphur in cystine. The sediment is found in company with a cystine-calculus, and also alone. It appears white, grayish, mixed with triple phosphates and phosphate of calcium; in acid urine with oxalate of lime.

With us this sediment is very rare; it is said that cystinuria has been observed frequently in several members of the same family.

Leucine and Tyrosine.

(See Fig. 4, Abnormal Constituents).

Leucine appears under the microscope in the form of spheres, of various sizes and more or less colored, that have the appearance of fat globules, They have sharp contours, and, with good light, show radii and delicate concentric lines.

Tyrosine forms very fine, short needles, crossing each other, collected in groups, and these groups lying upon each other so as to form crosses.

Sometimes this is found as a sediment, but more commonly we find globules of leucine mixed with it. Mistakes between leucine and fat globules can be prevented by ether, in which

fat is soluble, whilst leucine is insoluble. The crystals also dissolve in caustic potassa, but not in cold mineral acids.

Tyrosine crystals, as such, can be detected in two ways: by Piria's and by Hoffman's test. The first method consists in putting a small quantity of sediment into a watch glass and moistening it with 2 or 3 drops of concentrated sulphuric acid. After twenty or thirty minutes have elapsed, water is added, then calcic carbonate until effervescence ceases, then the whole filtered. If, upon the addition of chloride of iron, (free from acid) a violet discoloration takes place, the sediment was tyrosine.

The second method is simpler. Pour over the sediment water, and boil. To the boiling fluid a drop of a solution of nitrate of mercury is added. A red precipitate is formed, and the fluid has changed to pink or purple.

Leucine and tyrosine are rarely found, and then, nearly always in acute yellow atrophy of the liver or in phosphorus poisoning.

7. Fat.

One must be very careful not to consider the film of fat that is found upon urine, as a product of the urinary organs. In every case we can satisfy ourselves that it is the result of the introduction of the catheter. We must be equally cautious in regard to finely divided drops under the microscope. They are usually the result of some foreign admixture, as oil, in the vessels in which the urine has been preserved; fat upon the slide, milk, etc.

The statement that a high degree of fatty degeneration in the kidney will produce free fat globules in the urine, is one that we can not subscribe to, as a result of observation. *A*

priori this is not probable, as that part of the kidney that is fatty does not excrete urine; besides, requiring the assumption that the fat is separated from the kidney in the form of drops. That this idea is erroneous, can be shown at the post-mortem table. Emulsified fat is found in the chylous urine of the tropics, and the turbidity, inasmuch as it depends upon the fat, can readily be made to disappear by the addition of ether. It never forms a sediment, but, like cream, on account of its low specific gravity, it is found upon the surface of the urine. Under the microscope the fat shows globules with very sharp outlines: ether dissolves them. Cholesterin is found simultaneously with the fats; rarely, however, and then in its crystalline form. It is recognized by its characteristic crystal form; the transparent rhombic plates.

Galacturia is met with very rarely in temperate climates.

8. Earthy Phosphates.

(*a*) Amorphous.

In ammoniacal urine there is frequently found a layer of grayish-white sediment, which, by the beginner, may be mistaken for pus—this sediment consists of the precipitated earthy phosphates, *i. e.*, phosphates of calcium and magnesium. As has been stated, these salts are only dissolved in acid fluids; they, therefore, must precipitate as soon as the urea is split up, causing alkalinity of the urine. Under the microscope the earthy phosphates appear like granules of varying size, not resembling the urates, however, in their configuration. The differentiation can be easily effected by means of chemical tests. The urates, with the exception of urate of ammonia, occur in acid urine, whilst the earthy

phosphates (excepting the crystallized phosphate of calcium) are only found in alkaline urine. The reaction with litmus, then, is sufficient to solve the question of urates or phosphates. Heating causes the precipitate of urates to disappear, but increases that of the phosphates Upon adding caustic potassium or sodium the urates are dissolved; the phosphates remain unchanged.

The differentiation between pus and phosphates will be discussed further on.

All causes for alkalinity of urine produce this sediment, which is greater or less according to the quantity of dissolved earthy phosphates originally contained in the urine. Exceptionally, only, in diseases of the bladder and when great quantity of alkalies are taken internally, the urine is passed alkaline in reaction and then it is turbid, on account of the precipitation of the phosphates having taken place in the bladder; the rule is that the precipitation takes place after the urine has been passed. The so-called triple phosphate, in its characteristic form, is always mixed with the earthy phosphate in the sediment.

(*b*) Crystallized Phosphate of Calcium.

This substance ($PO_4HCa+2H_2O$) is found in pale, faintly acid urine, having a tendency to alkaline fermentation, usually very rich in phosphate of calcium. This sediment seems to occur as a result of individual predisposition; persons, otherwise perfectly healthy, are observed, whose urine in summer, always contains this sediment.

Under the microscope either single, wedge-shaped crystals are found or different arrangements of this crystal; several of them lying together, or having their apices directed to-

wards one point; or in the form of rosettes, the bases forming the periphery of the rosette. The form of the crystal is so characteristic that error is hardly possible. The triple phosphate never forms rosettes, and uric acid can always be distinguished by its color and insolubility in acetic acid.

IX. Phosphate of Magnesium.

In neutral or faintly alkaline urine, especially after the internal administration of carbonates, or mineral waters containing these, there are occasionally observed long quadrilateral plates, whose ends are rounded—basic phosphate of magnesium (probably $Mg_3(PO_4)_2+17H_2O$). If a drop of a solution of carbonate of ammonia (in 5 parts of water) is added, these plates become opaque, rough, and their corners fade. Phosphate of calcium is affected much more slowly, and does not become opaque, and the triple phosphate shows no change whatsoever with this test.

This sediment is very rare, and can only develop in urine that is *very much concentrated and, originally, of neutral or alkaline reaction*. If alkaline fermentation causes the alkalinity, then no magnesium phosphate can be formed, the ammonium magnesium phosphate always being the result.

X. Triple Phosphate.

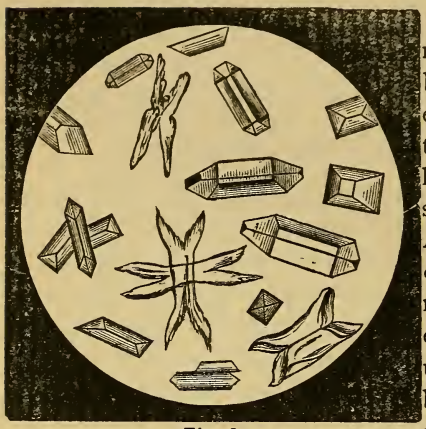


Fig. 8.
Triple Phosphate.

This substance is immediately recognized by its large, transparent crystals, that refract the light very much, having well-developed surfaces and angles. Among the manifold combinations of the rhombic form, frequently hemimorphous, the coffin lid, is best known. Mistake can be conceived only between common salt, oxalate of lime, and this crystal. Common salt, however, is never found in natural urine, only in urine concentrated by evaporation. The reaction with acetic acid prevents any error of diagnosis regarding the larger crystals of oxalate of lime, the triple phosphate always disappearing upon the addition of this reagent. The conditions producing the appearance of the triple phosphate are the same as those discussed under the head of earthy phosphates.

XI. Carbonate of Calcium.

Urine of most of the herbivora when voided is turbid, depending upon the separation of carbonate of calcium. Exceptionally, only, these conditions are found in the human being, the sediment forming some time after the urine has

been passed. The causes for this phenomenon are obscure.

The sediment, probably, never occurs alone, but mixed with earthy phosphates, and exceptionally forms dumb-bell crystals; most commonly it is coarsely granular or a fine powder. It is recognized by its effervescence and solubility upon the addition of mineral acids. This can be observed under the microscope. If a drop of hydrochloric acid is allowed to flow under the covering glass, small bubbles of gas (carbonic acid gas) will be seen to escape. This is never observed when earthy phosphates only are present. Before making the test, the sediment must be carefully washed upon a filter, to remove the carbonate of ammonium, which would show the same reaction as the substance tested for.

Organized Sediments.

1. Mucus.

Great quantities of mucus may be present in the urine and not be easily detected, on account of the slight difference that exists between the index of refraction of urine and mucus. It is only when urine has been allowed to stand for some time; when an abnormally great quantity of epithelium is present, or as a result of great and rapid development of bacteria, that mucus can be observed in the form of the nubecula already described.

In all cases in which these causes are not present, it becomes necessary to color the urine.

If albumen is not present, the mucus can be precipitated by alcohol to which tincture of iodine has been added; or acetic acid to which a solution of iodine in iodide of potassium has been added, is used. Acetic acid produces tur-

bidity in solutions of mucin which is not dissolved by excess of acid; disappearing, however, upon the addition of a few drops of hydrochloric acid.

If the turbidity disappears upon heating, then it was not caused by mucus but by the urates. Mucus does not show a characteristic picture under the microscope; but we find small bodies suspended in the mucus; crystals of oxalate of lime and uric acid, mucus corpuscles, (young cells) or epithelial cells of the bladder.

Mucus coagulated by acetic acid appears under the microscope in the form of a finely granular, striped mass, sometimes resembling casts.

In women the nubecula is usually greater than in men, because there is always present in the urine more or less mucus from the vagina—especially is this the case in leucorrhœa. As mucin does not dissolve in water, but swells up, it can be separated from urine by means of filtration. The mucus remains upon the filter, and, when it dries, appears like a varnish. Urine containing much mucus is not easily filtered, because the substance fills up the pores of the paper.

2. Epithelium.

In treating of mucus we saw that there are suspended in it young cells that were called mucus corpuscles. But cells of other description that formerly lined the urinary apparatus or formed part of the glanduar substance of the kidneys, also appear in urine.

Their forms in the urine are not as manifold as when taken directly from the organs in the cadaver, depending upon the fact that the urine alters the shape of the cells.

The forms of the cells may be divided into three classes :

1. Round cells.
2. Conical cells and cells with processes.
3. Flat cells.

1. The round cells come from the uriniferous tubules and the deeper layers of the membrane lining the pelvis of the kidney. In their original form they are more or less flattened, depending upon their arrangement. Influenced by the urine they swell up and represent spheres. They have a well-developed nucleus, and by it are differentiated from pus. Pus cells are granular, and only upon the addition of acetic acid show a nucleus. Epithelial cells have but one nucleus, pus cells two or three, rarely more ; finally epithelial cells are larger.

Fig. 9.—*a*, Epithelia from male urethra; *b*, from the vagina; *c*, from the prostate gland; *d*, from Cowper's glands; *e*, from Littre's glands; *f*, from the female urethra; *g*, from the bladder.

In acid urine epithelial cells are preserved for some time, but when the urine becomes neutral or alkaline they appear larger, nearly hyaline, in that the granular protoplasm collects around the excentric nucleus, and, finally, are completely dissolved. The epithelium of the male urethra can not easily be distinguished from that of the kidney by means of the microscope. The chemical reaction of the urine must here be taken into consideration. If the urine contains

albumen the cells originate in desquamation in the uriniferous tubules; this not being present the cells are, in all probability, from the urethra.

The cells from the prostate, Cowper's and Littré's glands are like those of the urethra and can not be distinguished from them by means of the microscope; in all probability they rarely occur in the urine. Fused with mucus and pus they form the shreds found in gonorrhœa.

The conical cells and cells with processes, in the majority of cases, come from the pelvis of the kidney; very fine and delicate cylindrical cells may be from the accessory organs of the male urinary apparatus, but these are quite rare. They are commonly twice as long as they are broad and tapering towards one extremity. The second variety may have either one or two processes (unipolar and bipolar cells). The occurrence of these must not be considered as a symptom of neoplasmata, as is laid down in many of the older text books.

3. Flat cells either originate in the bladder or in the vagina.

As the name indicates their form is flattened. Usually they are irregular, polygonal, having rounded edges and a dark, sharply-defined nucleus that is nearly central. The latter protrudes somewhat and a cell of this sort when seen in profile appears thicker in the middle, like a spindle-shaped cell.

It is only with difficulty that epithelium of the bladder can always be distinguished from epithelium of the vagina. The cells from the bladder are more delicate, and usually are found singly; those from the vagina are tougher—sometimes seem like scales; nearly always in larger or smaller

flakes, above all in layers, a thing that can not occur with the epithelium of the bladder.

The yellow discoloration of the nuclei of various epithelial cells in jaundice is of interest. If a drop of fuming nitric acid is allowed to flow slowly under the thin covering glass, the well-known play of colors of Gmelin's test (green, blue, violet,) is produced (Ultzmann).

III. Pus Corpuscles.

Pus corpuscles in urine have the same microscopical characteristics that are possessed by those from a suppurating wound. They are round cells, twice as large as red corpuscles of the blood, and have a granular exterior, which covers over the nuclei. These will appear immediately, however, upon the addition of acetic acid. The granular appearance disappears, the corpuscles swell, and the multiple central nuclei become visible. One rarer form differs from this common form; the corpuscles are not round, but have many processes, so that they resemble the amœba.

Especial changes are undergone by pus corpuscles in alkaline urine, due to the action of carbonate of ammonium. They are fused, melted together, and the microscope then reveals an homogeneous mass with nuclei. Such pus forms an adherent, vitreous mass, which can only be poured out as a whole, somewhat like the white of egg.

Especial attention must be called to the fact that these masses are neither albumen nor mucus. The former *never* forms a sediment, and the latter *never* forms adherent masses. If pus is present, there must also be present pus-serum, and therefore albumen. In every case, then, the albumen test discovers albumen, which is not the case with mucus.

The number of pus corpuscles varies very much. In some urine so few are found that they are not detected by the naked eye; in others they are so numerous that a yellowish or grayish-white precipitate of the height of a finger is found.

In acid urine it is possible to confound the urates with pus; in alkaline, the phosphates. The former have already been differentiated in another place. The phospates disappear upon the addition of a few drops of acetic acid, the pus does not.

But we have a positive test, without using the microscope, for pus—Donné's.

Pour the urine from the sediment, add to the latter a piece of caustic potassa or soda and stir with a glass rod. If the sediment consists of pus it will lose its white color, will become green and vitreous, denser, and finally be reduced to an adherent mass, *i. e.*, it assumes the appearance of pus in ammoniacal urine. As there exists in urine no other body that causes this reaction, the test is a positive one. Only when the quantity is small we will not obtain a mass—the sediment, however, disappears and in its stead we have a mucilaginous fluid.

Not infrequently we find in the sediment pus corpuscles that have been destroyed (detritus), blood corpuscles, epithelium, etc.

4. Blood Corpuscles.

The presence of blood corpuscles, even in small numbers, can be detected without difficulty by the microscope. When the urine appears of a brownish-red tint, suspicious of blood-coloring matter or blood corpuscles, it must be allowed to

stand for some time in order to permit the light corpuscles to come down as a beautiful red sediment (frequently only a trace).

In acid urine they retain their characteristic shape for a long time. They represent small discs that possess shading corresponding to a central depression. If seen in profile they appear bi-concave. They are always separate (except in excessive hemorrhage from the bladder), when they are arranged in money-roll order and appear reddish, slightly tinted with green.

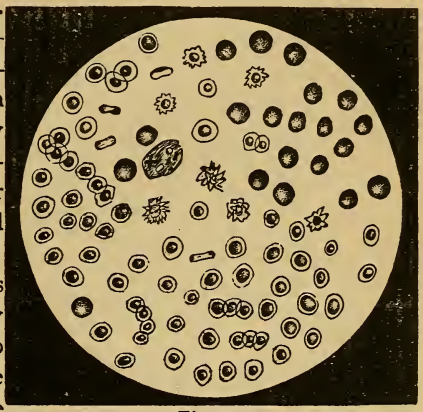


Fig. 10.
Blood Corpuscles.
To the right and above—red corpuscles acted upon by diluted urine; to the left, acted upon by salts; in the middle, the crenate form; and below, the normal.

This original form is subjected to many changes, according to the fluid in which the blood corpuscles are found. If the urine is very much diluted, especially when beginning to be alkaline, they swell up. The depression disappears, the blood corpuscle becomes spherical and seems smaller than before. The shading in the centre disappears with the depression, but appears at the periphery, by which it is recognized as a sphere.

When acted upon further, the corpuscle becomes less distinct, appears as a small bubble, then as a mere shadow, and finally disappears altogether.

By the action of salts the blood corpuscles become smaller

and crenate. The latter form is sometimes observed in urine, by the side of the normal. They seem to be produced by small crystals whose corners lift up the surface of the blood corpuscle. Sometimes the corpuscles are not round, but oval, of various sizes, and twisted into the form of a cup.

In haematuria, accompanying parenchymatous diseases of the kidney and bladder, we find, nearly constantly, spherical corpuscles of varying size. Very small, even dust-form corpuscles (mycrocytes), are found in these cases by the side of normal and large forms (macrocytes).

When blood corpuscles are present, even in very small quantity, albumen can always be detected.

If the corpuscles are dissolved by alkaline urine, the blood coloring matter (haemo- and methaemo-globine) can be detected according to methods described elsewhere.

The etiology of bloody urine will be discussed in Chapter VIII.

V. Casts.

Of the greatest importance for the diagnosis of kidney disease are those structures, disclosing their origin by their form—the uriniferous tubules, and called casts.

In searching for these structures in urine, the greatest caution is necessary, so that they are not overlooked. On account of their low specific gravity they remain suspended in the urine for a long time, in addition to which they always appear in urine containing albumen, in which everything suspended will settle slowly.

The first condition is that the urine be allowed to stand for several hours, then carefully decanted and the remainder poured into a wine-glass and allowed to stand for one or two

hours. The last drops of the sediment are put under the microscope for examination. One must not be satisfied with one preparation, as it is frequently necessary to examine several, otherwise the casts elude discovery. On the other hand, one must guard against mistaking other structures for casts. Beginners are apt to consider every cylindrical arrangement of phosphates or urates, especially when deposited in mucus, as finely granular casts.

Casts are usually accompanied by albuminuria. As well as there occur cases in which albumen exists without the presence of casts, equally well casts are found without albumen. Examples of the first anomaly are found in albuminuria of interstitial nephritis, in the amyloid and the hyperaemic kidney; example of the latter is any serious inflammatory process in which the casts may precede the presence of albumen by from 12 to 24 hours.

Amongst the many varieties of casts, the following can be considered the typical forms: 1, the coarse fibrine cast; 2, the finely granular cast; 3, the hyaline cast; 4, the epithelial cast; 5, the so-called uric acid cast; 6, casts of bacteria and cocci.

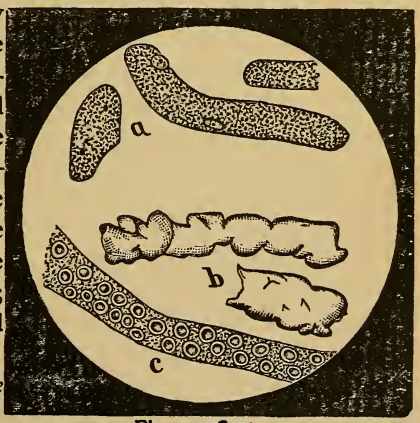


Fig. 11.—Casts.
a, Finely granular; *b*, waxy; *c*, blood-casts.

1. *The Coarse, Fibrine Casts* are roller-like, coarse, frequently cork-screw coagula, with sharp outlines, and of yellowish or

brownish-yellow color. Their diameter, greater than that of any cast, indicates that they are formed in the lowest part of the collecting tubule, near its opening into the papilla. Not infrequently epithelial cells adhere to them. Bloody casts may be considered as a variety of this form, consisting of coagulated blood from rupture of the glomeruli. They are always dark brown, and, in some cases, seem to consist entirely of blood corpuscles; in other cases, we observe in one part of the cast coagulated fibrine only, and in the other only blood corpuscles. This form is always accompanied by blood corpuscles in the sediment. (See Fig. 11, *c*.)

2. *The Finely Granular Casts* (Fig. 11, *a*) are more delicate than those described above. They, apparently, are derived from the smaller tubules. They possess distinct contours, and, as their name implies, are finely granular throughout their whole extent. They are straight and rounded off like a finger either at one or both ends. They are of the same diameter throughout, narrowed at one point, or tapering at one end. In their granular structure, also, many modifications are observed. In places they are coarsely granular, in others this appearance is nearly lost so that they approach the hyaline casts, to be described presently (half-granular casts). Sometimes distinct fat globules are present. The addition of acetic acid, in some cases, causes a decided clearing up; in others, no effect at all is produced. The color of these casts is a faint grayish yellow.

Both forms retain their shape for a long time in acid urine, losing it gradually in alkaline urine.

3. *The Hyaline Cast* (Fig. 12, *b*) is partly of the size of the granular casts partly, much smaller. They are either perfectly straight, frequently of considerable length, or curved. Whilst

some produce the impression of a solid, others seem like tubes with very delicate walls; the one being decidedly cylindrical, the other like tape. Not infrequently casts are found that are spiral, with one or more turns. With the larger ones, distinct outlines can be observed; the smaller appear like shadows under the microscope, and can be separated from their surroundings only with difficulty. In such cases it becomes advisable, in order to bring out the outlines, to add a few drops of a solution of iodine in iodide of potassium or aniline violet. By means of this, the casts appear yellowish (or bluish-violet), and can easily be distinguished. They show no signs of granulation, but are pellucid and hyaline. On account of the size of those formed like tapes, we are justified in thinking that they come from the finest ramifications of the uriniferous tubules, perhaps from the ascending limb of Henle's loop. Hyaline casts disappear very rapidly in alkaline urine.

Fig. 12.—Casts.

a, Uric-acid casts; *b*, hyaline; *c*, epithelial cast.

4. *Waxy Casts* (Fig. 11, *b*), nearly always, are of the same breadth as the granular, perfectly vitreous, refracting light so much that their outlines stand out somewhat like the crystals of the triple phosphate, or similar clear crystals. They are

straight, with sharply-broken ends or tortuous. Their surface is sometimes wavy, as if the cast were made up of masses of colloid substance that have become fused. In places there is noticed distinct cleavage, that produces the impression, as if a gelatinous mass had been compressed and given way. They show the amyloid reaction, and possess greater resistance than other casts. This form is very rare, and, up to the present, only found in amyloid degeneration and tuberculosis of the kidney.

5. *Epithelial Tubes and Casts* (Fig. 12, *c*). There are processes in which the epithelial lining, in toto, is stripped from the membrana propria of the tubules, and on account of the *vis a tergo* of the urine, or a fluid exudation is washed from the tubules. These structures, made up of epithelial cells, and hollow, are called tubes. In the same sediment, or without the presence of these tubes, are found casts that are covered with epithelial cells, as if with the finger of a glove. The cells always are cloudy, somewhat swollen, and rarely possess sharply-defined outlines. Frequently, they are so much enlarged that they resemble more a finely-granular mass, which, however, can be seen to be made up of cells by the nuclei that are present at regular intervals.

Amongst epithelial casts are found such, in which the epithelial layer is wanting in places where the congealed exudation can be observed. In others the central exudation protrudes beyond the epithelium.

6. *Uric Acid Casts* (Fig. 12, *a*) differ very much from the preceding in regard to their structure, and can only be classed with them on account of their common origin. These casts are found most commonly during the first days of life in those children that suffer from uric acid infraction. There can be

observed, in the urine, as well as in the liver of such patients, small, red bodies, which, under the microscope, show a cylindrical structure. They are made up of balls of urates, not as we would infer from their name of pure uric acid. They are brownish-red, show a decidedly granular structure, and vary very much in regard to size. Treated with caustic potassa, ammonia escapes, and the casts disappear. There are also found parts of casts.

7. *Casts* made up of *Bacteria* and *Cocci* only occur in suppurating interstitial nephritis, and only then, when the disease is complicated with emboli of bacteria in the uriniferous tubules (Nephritis Parasitica—Klebs).

These casts are found of the shape and size of the large fibrine casts. They come from the collecting tubules, and sometimes are divided dichotomously, showing that they originate where two large tubes unite. They are made up entirely of cocci and bacteria. On account of the bacteria being at perfect rest, these casts resemble the coarse granular; but high powers make mistake impossible.

Amongst the forms already described, several will not be found that are mentioned in text-books; because we have not observed them, and therefore must conclude that they are exceedingly rare. We refer here to casts of pus cells, not to be mistaken for those short plugs closing up the mouths of the tubules at the papilla and characteristic for chronic pyelitis; furthermore, casts made up of oxalate of calcium, and casts having uric acid imbedded in them. It is very common to find casts having oxalate of calcium or uric acid adhering to them, but these are not imbedded in the cast, and therefore have been accidentally formed outside of the uriniferous tubule.

IX. Fungi.

In urine are found forms of fungi partially developing; some of these are frequently found, others are accidental admixtures.

Those forms that are most commonly seen are: 1. Bacteria. 2. The Yeast Fungus. 3. Sarcinae. 4. Oïdium lactis. 5. Spores and fragments of penicillium glaucum.

1. *Bacteria*, principally found in alkaline urine; by different authors, have been classified as vegetables or animals, and therefore been differently named, as vibriones, monas crepusculum, microzyma, etc. It seems settled now that they are to be considered as fungi belonging to Nägeli's schyzomycetes. They differ very much in appearance, and, practically, it is well to give to the different forms different names, according to A. Vogel, always bearing in mind, however, that it is the same fungus.

(*a*) *The Monad.* Round, puncti-form bacteria, either at rest or vibrating. Care must be taken not to take earthy phosphates having molecular motion for these fungi. Granules of a dead body have motion, but do not change their place in the field like the bacteria.

(*b*) *The Rod.* Very small rods, hardly as long as the diameter of a red blood corpuscle, whose thickness is to small for measurement. Both extremities are somewhat dilated. They are at rest or in motion.

(*c*) *The Leptothrix, or Chain Form*, are long chains, frequently extending over the whole field, and can be distinguished from the vibriones by their length. With high powers their structure can be observed. They rarely move, and then very slowly.

(*d*) *The Vibrio*, originating in the former. Several rod-bacteria adhere to each other, and move about either in

spirals or in that the members at the ends vibrate like the tail of a fish. Frequently they move with great rapidity.

(*e*) *The Zooglea Form.* Masses of punctiform bacteria, held together by a gelatinous mass, and looking like a mass of earthy phosphates imbedded in mucus.

All these forms can be observed in one urine, even in one preparation.

Fig. 13.—Fungi.

a, Micrococci and vibriones; *b*, Sarcinae; *c*, Saccharomyces urinae; *d*, Yeast-fungus; *e*, Penicillium glaucum.

2. *The Yeast Fungus—Saccharomyces Urinae.* Single, vesicular cells of the size of red corpuscles, somewhat oval. Commonly arranged in a beaded form, or as one large cell having several smaller ones resting upon it. Their number is usually much smaller than that of bacteria; they are found principally in acid urine, and in warm weather this fungus is very like the yeast fungus of beer (saccharomyces cerevisiae), without being identical with it. In the urine of diabetes the same form, better developed, is found.

3. *Sarcina.* Resembles the sarcina ventriculi, but is much smaller. They are arranged in groups of 2, 4, 8, etc., cells, and where they are collected in the form of cubes, resemble very much, bales of goods.

Urine in which this form is found is usually alkaline, and we therefore also find phosphate of calcium and the triple

phosphate. They are usually observed for weeks, even months, in the urine of the same patient.

4. *Oidium Lactis.* Long cells, to be recognized by the nuclei, which are in rows, at regular intervals from each other. Not infrequent in fermenting diabetic urine. Besides those mentioned, we find in urine sporules of

5. *Penicillium Glaucum*, in partial division. Sometimes they are mixed with fine urates, so that they appear like fur and brownish-red; or their development has progressed, and we find a network of fine thallus threads.

The seeds for the development of all these forms, as a rule, are mixed with the urine outside of the bladder. But this rule has exceptions. The sarcina is voided with the urine; this is sometimes the case with bacteria, but the cause is to be found in unclean catheters and sounds. We have rarely met with cases in which an instrument had not been introduced into the urethra or bladder. Whether these structures play a rôle in fermentation and the reaction of urine, is very doubtful. The small chains appear not only in alkaline urine, but everywhere where albuminous substances undergo decomposition. We find them, therefore, in secretions from a variety of ulcers, in bad pus, in passages from cholera patients, etc.

Formerly a membrane, named kyesteïne, made up of fungi, phosphate of calcium, triple phosphates, and sometimes animal organisms, was held to be characteristic of the urine of pregnant women. This is also found upon the urine of males, and therefore is of no value as a sign of pregnancy.

VI. Spermatozoa.

Spermatozoa, when viewed with high power, appear as small, spherical structures, with a hair-like tail. In urine

they are rarely found in motion. Urine containing sperm frequently shows small, cloud-like bodies, which, under the microscope, are seen to consist of spermatozoa imbedded in a finely granular mass. The spermatozoa are very light, and therefore require from 6—12 hours before they are found in the sediment. They may be found several days after the urine has been passed, and under the following conditions:

1. After coitus, nocturnal emissions, etc., when semen has remained in the urethra and been washed out by the urine.

2. In spermatorrhœa; in grave attacks of typhus, involuntary passages of semen have also been observed.

In the urine of women, spermatozoa are found after coitus, and may be of medico-legal importance.

VII. Parts of Cancer.

Two forms of cancer parts are observed, both very rarely, however. (*a*) *Single cancer cells.* (*b*) *Pieces of cancer tissue.* (*a*) *The cells* vary, frequently unusually large, caudate cells, with multiple nuclei. Sometimes so-called nests are observed. We must be cautious not to mistake caudate cells from the kidney (pelvis) for cancer cells. The cells correspond with the epithelial covering of the cancer granulations, and commonly originate in the bladder. We are justified only in making a probable diagnosis when these peculiar cells are present in great quantity.

Fig. 14.—Cancer Tissue and Cells.

(*b*) *The Stroma of the Papillary Cancer* occurs in various forms in the sediment. Either it is well preserved, and then the diagnosis is easy, or it is necrotic, and then the diagnosis becomes exceedingly difficult. When well-preserved, we see a dentritic vegetation, covered by a single layer of epithelial cells, and consisting of an ecstatic blood-vessel. This is a rare picture. More commonly we find the dead, modified papillæ, and their diagnosis is exceedingly difficult. The dentritic form can no longer be verified, the epithelial covering has been destroyed, and the papilla itself infiltrated with pus corpuscles. In this formless mass, however, occasionally structures are found that make the diagnosis much easier. They are:

When treating the necrotic tissue with glycerine, beautiful crystals of hæmatoidine. They appear of a yellowish-brown color, either in the form of rhombs or bundles. This tissue, treated with fuming nitric acid, gives, under the microscope, the characteristic reaction for bile coloring matter. Hæmatoidine is only found in old extravasations of blood; if we discover it imbedded in necrotic tissue, the diagnosis of old hemorrhage is positive, and this has only been found in papillary tumors. This form is found only in acid urine.

Another form of crystal, which we have found only in necrotic cancer tissue, and only in acid urine, is a rare form of oxalate of calcium; dumb-bells crossing each other, sometimes spherical.

Sometimes we find with low powers flakes of dense, dark, tubular, branched structures. These are the minute blood-vessels.

If the urine is highly alkaline, the papillæ are covered

with phosphates, and so much changed that a diagnosis is next to impossible. One examination does not suffice for a recognition of this disease.

VIII. Entozoa.

As yet we have never had occasion to see parts of entozoa in the urine. According to other authors the hooklets of echinococci are said to occur in the sediment. But we have observed both hooklets, and also a piece of an echinococcus-sac with the animals, in fluid drawn from a tumor of the kidney, and it is possible that when this tumor breaks into the pelvis of the kidney, hooklets would be found in the urine.

In the tropics haematuria, produced by entozoa, is frequently observed. The entozoa, most important in this respect, are the distoma haematobium or the bilharzia haematobia. They probably migrate from the intestine into the venous plexus of the prostate gland and there lay their eggs. These are of oval form, having at one end a sting-like process and plug up the smaller vessels in the bladder. There is produced catarrh of the bladder, with hemorrhage, and the eggs are discharged with the urine.

It is hardly worth mentioning that a great many accidental impurities, having no relation to the urinary apparatus, may be found in the urine.

Pieces of feathers, of wood-cells, of plant parenchyma (tobacco leaves, for instance), dust, very fine fibres of cotton, silk, etc. Neither is it necessary to mention that care must be taken not to mistake substances upon the slide or their cover, or air bubbles, for sediments.

Addendum.

Concretions.

By concretions we mean hard, stony bodies, made up either of normal or abnormal constituents of urine. They vary very much in size. We find them as large or larger than a fist, and then others that can only be detected by means of the microscope.

Every concretion, whether large or small, must show a deposit of molecules in layers and must be more or less rounded. The only exception is the cystine calculus, which upon section shows a crystalline structure.

If we wish to judge, then, upon this point, we must take either a lens or a microscope.

We frequently find concretions of uric acid that, with the naked eye, might be mistaken for a conglomerate of uric acid crystals (rosette). Also concretions of calcic carbonate are found which show the arrangement in layers only when a power of 100 or 200 diameters is used.

The small concretions usually come from the kidney, the larger ones from the bladder.

Calculi are either made up solely of one constituent or of several, arranged in layers. Thus uric acid calculi usually consist throughout of uric acid, or its salts; cystine calculi of cystine; while the oxalates frequently have a nucleus of uric acid and an outer layer of phosphates, and the phosphates a nucleus of uric acid.

It is immaterial whether one or more constituents are used for the formation of the calculus; we are always in a position to distinguish the nucleus.

In order to examine the structure of the calculus it is necessary to cut it by means of a fine watchmaker's saw. The innermost layer is the nucleus, which varies in size from a millet seed to that of a pea or over, and shows to greatest advantage when surrounded by a layer of a different structure from its own.

The nucleus is the most important part of the calculus, as it alone gives definite knowledge regarding the genesis of the stone. If we find an uric acid nucleus in a phosphatic calculus, we will know that calculus formation was caused by uric acid; if we find a foreign body, as a piece of catheter or bougie, we may know that this was the primary cause.

From a surgical stand-point calculi are divided according to their principal constituent: thus calculi of urates, oxalates, phosphates, and cystine. This division is of great practical importance, for, if a surgeon states that a calculus is phosphatic, he, at the same time, implies that it is soft; if oxalate or urate, that it is hard.

But as these are calculi, made up of three or more different layers, it is better to divide all concretions by taking for a basis their nuclei, and in this way form two groups.

One group contains all those calculi whose nuclei are formed by the sediments of acid urine; the second those whose nuclei are either foreign bodies, coagula of blood, or constituents of alkaline urine.

This division agrees with what is called primary and secondary calculus-formation: primary being the first and secondary the second group, to which latter is added the incrustation of a calculus from the kidney in the bladder. Primary calculus-formation takes place only in the kidney; secondary, nearly always in the bladder.

A separate class is formed by the so-called metamorphous calculi. They consist of earthy phosphates, and form a homogeneous, porous mass. They are always the result of a purulent process, continuing for years, in which the sediment of acid urine has been dissolved by the alkaline pus and substituted by the earthy phosphates.

Primary formation is begun principally by uric acid, as the greater number of calculi of the bladder possess a nucleus of uric acid.

In 545 calculi from the bladder, Ultzmann has found the nucleus to consist as follows:

Uric Acid,	441	or 80.9%
Oxalate of Calcium,	31	or 5.6%
Earthy Phosphates,	47	or 8.6%
Cystine,	8	or 1.4%
Foreign Bodies,	18	or 3.3%

Analysis.

Every calculus must be divided into two equal parts with a saw. The dust from the sawing must be mixed, collected, and examined by the key which follows. In this way all the principal constituents are discovered, but not their arrangements.

In order to determine this, one-half is polished upon a glass plate until the various layers can be easily distinguished. From each layer sufficient quantity is scraped off with a penknife and this is examined separately. An illustration will make this clearer.

It has been determined that the ½ of a calculus is

made up of ⅔ inorganic (non-combustible) and ⅓ organic substances. Furthermore the following substances have been detected: uric acid, oxalic acid, phosphoric acid, calcium, magnesium and ammonium.

We now polish and find three layers. The nucleus, by the proper test, is found to consist of uric acid, the dark-brown middle layer of oxalate of calcium and the white outer layer of phosphate and carbonate of calcium and magnesium salts.

The method for analysis is as follows:

A few millegrammes of the powder are taken and heated to redness upon platinum. We must observe if there is left a deposit upon burning or not; whether there is produced a visible flame or not; whether the substance crackles (oxalate of calcium), and whether there is produced a characteristic odor.

I. *No* deposit left upon *burning*, there may be present the following substances: uric acid, urate of sodium and of ammonium, xanthine, proteine and cystine.

1. *Proteine*, when burnt, has a yellow, luminous flame and causes an odor like burnt feathers or hair.

2. *Cystine* burns with a faint bluish white flame, and produces a penerating odor of burning fat and sulphur. The powder is soluble in diluted ammonia and upon evaporation shows the characteristic crystal.

3. *Xanthine*, with the murexide test, produces a pomgranate-yellow color and burns without a visible flame.

4. *Uric acid*, *urate of sodium* and *urate of ammonium* give the characteristic murexide reaction.

(*a*) *Urate of sodium* can be distinguished from urate of ammonium and uric acid by the fact that at the spot upon

the platinum where the urate was burnt there remains a slight haziness, a piece of red litmus paper moistened and put upon this spot will immediately turn blue where it touches the haziness, due, probably, to the presence of carbonate or hydrate of sodium, formed by decomposition of urate of sodium.

(*b*) *Urate of Ammonium* can be distinguished by the detection of ammonium. Some of the powder is moistened with caustic potassa; over the mixture is suspended a piece of red litmus, which will be turned blue by the escaping ammonium.

(*c*) *Free Uric Acid* gives negative results with both of these tests.

II. If the powder is *incompletely burnt*, or not at all, it consists principally of salts of calcium and magnesium. We may then have the following that form calculi: oxalate of calcium, carbonate of calcium, phosphate of calcium and the triple phosphates.

1. *Oxalate of Calcium* does not produce effervescence when hydrochloric acid is added. When heated we notice a peculiarity in glowing and a crackling sound. The oxalate has been converted into a carbonate and addition of hydrochloric acid will now cause decided effervescence.

2. *Carbonate of Calcium* will effervesce, without being heated, upon the addition of hydrochloric acid.

3. *Phosphate of Calcium* and *the Triple Phosphate* neither effervesce before nor after heating. The powder, after heating, dissolves entirely in hydrochloric acid. If to this solution caustic ammonia is added until alkalinity has taken place there is found a flaky precipitate of amorphous basic phosphate of calcium and crystalline triple phosphate. The latter, under the microscope, consisting of crystals in the form of stars or crosses.

CHAPTER IV.

Reagents and Apparatus for the Approximate Examination of the Constituents of Urine.

It is best to have wide-necked bottles, with ground stoppers, holding 250 c. c. of fluid. We give the reagents in the form of prescriptions:

(*a*) Acids.

1. Acid. hydrochloric. C. P., 200.00.
2. Acid. sulphuric. C. P., 200.00.
3. Acid. nitric. C. P., 200.00.
4. Acid. acetic. C. P., 200.00.

(*b*) Bases and Salts.

5. Potass. fus. pur., 100.00.
   Aquæ destillat., 200.00.
6. Ammon. pur. liquid. 100.00.
7. Barii chlorid. cryst., 30.00.
   Aquæ destillat., 200.00.
   Acid. hydrochloric. 10.00.
8. Plumbi acetat. cryst., 30.00.
   Aquæ dest., 200.00.
9. Cupri sulphat., 30.00.
   Aquæ destillat., 200.00.
10. Magnesiæ sulphat.
    Ammonii chlorid. pur. āā, 30,00.
    Aquæ destill., 200.00.
    Ammon. pur. liquid, 50.00.
11. Argenti nitrat., 5.00.
    Aquæ destill., 40.00.
12. Red and blue litmus paper, cut in strips.

Besides the preceding, which are absolutely necessary, the following can be kept for special cases: distilled water, choride of iron, chloride of zinc, basic acetate of lead, nitrate of mercury, subnitrate of bismuth, fuming nitric acid, nitrite of potassium, starch, chloroform, ether, alcohol, iodine dissolved in iodide of potassium, glacial acetic acid, chloride of sodium, etc.

APPARATUS.

1. Six test-tubes and stand.
2. Ten wine-glasses (such as are used for sherry wine).
3. Cylinder glasses, containing 100, 200 and 300 c. c.
4. A graduated cylinder.
5. A flask holding 100 c. c. with cork perforated by a glass tube.
6. A washing bottle.
7. An urinometer (areometer).
8. A spirit lamp.
9. Two small porcelain dishes.
10. A stand of brass, with two rings.
11. Filtering paper.
12. Four funnels.
13. Glass rods.
14. A microscope.
15. A glass vessel, holding 3,000—4,000 c. c.

Watch glasses, beakers, pipettes, and for quantitative purposes apparatus for volumetric analysis are necessary.

CHAPTER V.

Quantitative Detection of Urinary Constituents.

One condition is necessary for all quantative estimations; the exact collection of all the urine passed within a given time. The urine is usually collected during 24 hours, and in order to prevent its mixture with feces, it is to be passed before defacation.

We can not multiply the quantity of one hour, in order to estimate that of any number of hours, as the quantity of urine varies with different parts of the day.

Urine is collected in graduated cylinders. If we wish to find the average of excretion of any patient, it is necessary to collect the urine for several successive 24 hours; then average.

I. Estimation of Acidity.

In order to estimate the degree of acidity a solution of hydrate of sodium is added until neutral reaction sets in; then compare how much of any acid (best oxalic acid) is required to neutralize the quantity of alkali used.

(*a*) Test Solution.

There is necessary a $\frac{n}{10}$ solution of sodic hydrate, which contains 0.0031 grammes NaO in 1 c. c., neutralizing 6.3 millegrammes of crystalized oxalic acid.

(*b*) The Test.

Measure off 100 c. c. of urine in a beaker, then add, with

a burette, the above solution until the reation to litmus is negative. The number of c. c. used is multiplied by 0.0063. The product shows the acidity of 100 c. c. of urine reduced to oxalic acid.

II. Total Solids.

10 c. c. are evaporated to dryness in a porcelain dish, that has been weighed, over the water bath, this kept at 100° C. in the air-bath for an hour, then allowed to cool under a dessicator, and weighed. Again dried and dessicated and weighed, and this operation repeated until no diminution in weight is observed. The difference between this weight and that of the dish represents the weight of the solids in 10 c. c. of urine. Unfortunately, the result is not accurate on account of the reaction of the acid sodic phosphate upon urea, producing, at 100° c., carbonic acid gas and ammonia, which are lost.

Usually the approximate means are sufficiently exact for the practicing physician. If not, the method of Neubauer ought to be used. (See Neubauer and Vogel, Analysis of Urine.)

III. Urea.

1.—The Method of Liebig.

(*a*) *Reagents.*

1. *Barium Solution.* 1 vol. of saturated (cold) solution of barium nitrate is mixed with 2 vol. cold, saturated solution of barium hydrate.

2. *Titrate for Urea, i. e.*, solution of pure mercuric nitrate, of the concentration that 71.48 gr. of pure mercury, or 77.2 gr. of mercuric nitrate; dried, at 100° C., are contained in 1 litre. (For preparation see Neubauer and Vogel).

Solution of Sodic Carbonate. For Raudenberg's modification, acid sodic carbonate must be used. This is stirred up in water, after having been rubbed up finely and washed by small quantities of water until turmeric is no longer turned brown.

(*b*) The Test.

With a pipette 40 c. c. of urine are taken, and 20 c. c. of

the barium solution added. A precipitate of phospates and sulphates will result. Allow to stand, and then filter into a dry vessel through dry paper. The filtrate is composed of one-third barium-solution and two-thirds urine, from which the sulphates and phosphates have been withdrawn. Of this mixture 15 c. c. are taken and poured into a dry vessel (only two-thirds or 10 c. c. are urine). Now allow the solution of mercuric nitrate to flow into the urine from a burette. Having used as many c. c. of the solution as are indicated by the last two figures of the specific gravity of the urine examined (thus 13 c. c. if sp. gr. is 1.015), it is necessary to see whether or not the limit has been reached.

Take a drop from the mixture and put it into a porcelain dish, add to this a drop of sodic carbonate. If a rusty zone is produced, where the fluids meet, continue to add the test fluid; if, however, this is pale, cease, for the work is completed.

The chemical process is as follows: Upon the addition of mercuric nitrate $Hg(NO_3)_2$, it first seeks the chlorine, of the common salt in urine, forming $HgCl_2$ (corrosive sublimate).

$$Hg\begin{cases} NO_3 \\ NO_3 \end{cases} + \begin{matrix} NaCl \\ NaCl \end{matrix} = HgCl_2 + 2NaNO_3$$

The $NaNO_3$ remains dissolved, but the $HgCl_2$ is precipitated, the solution being alkaline. After all NaCl has been converted into $HgCl_2$, the mercuric nitrate forms a combination with the urea, by which NO_3 is liberated, which, upon the addition of sodic carbonate, takes the place of the carbonic acid; this escaping in fine bubbles. $NaNO_3$ does not change the color of the precipitate in the porcelain dish. But if the limit has been reached, where all the mercuric nitrate is bound to the urea, and a drop of the mixture with urine is added to sodic carbonate, mercuric oxide is precipitated, at the same time $NaNO_3$ being formed, and CO_2 escaping:

$$Hg(NO_3)_2 + Na_2CO_3 = HgO + CO_2 + 2NaNO_3.$$

HgO is precipitated as a brownish powder, which, as we now comprehend, forms the limit test for the reaction.

Having completed titration, the burette is allowed to stand *for a few minutes*, and we then read off how many c. c. have been used.

The fluid is so arranged that 1 c. c. satisfies 10 millegrammes of urea, exactly. If we had used 20 c. c. there would be present 200 mgr. of urea in the mixture (15 c. c.), which was made up of 10 c. c. urine and 5 c. c. barium fluid. From this can be computed, without difficulty, how much urea is passed in 24 hours.

1. As the test fluid is fixed for a 2% solution of urea, we can only obtain accurate results when for 15 c. c. of a 2% solution of urea, there is used exactly 30 c. c. of the mercury solution, of which 1 c. c. represents 10 mgr. of urea exactly.

Every c. c. of the solution requires for the satisfaction of 10 mgr. of urea, 72 mgr. HgO. In order, however, to produce the terminal reaction, there must be an excess of HgO. According to Liebig, this amounts to 5.2 mgr. for 1 c. c. of the solution, for 30 c. c. $30 \times 5.2 = 156$ mgr. If, now, to 15 c. c. of a 2% solution of urea, 30 c. c. of the solution are added, the mixture amounts to 45 c. c., in which there are 156 mgr. of HgO in excess, *i. e.*, 3.56 mgr. for each c. c. In order to effect a positive terminal reaction, then, it is necessary to have in each c. c. of mixture 3.46 mgr. of HgO in excess.

If the 15 c. c. of urea solution have 3.5% urea, 52.5 c. c. of the mercury solution would be required. The quantity of the mixture then would be 15 c. c. + 52.5 c. c. = 67.5 c. c.; in the 52.5 c. c. of solution is present $52.5 \times 5.2 = 273$ mgr. of HgO in excess, in every c. c. of the mixture; therefore, 4.04 mgr. But the termination of the reaction takes place with 3.46 mgr. we therefore have 0.58 mgr. too much. In this way the terminal reaction sets in too early.

If the solution only contains 1% of urea, the error would be in the other direction.

In order to eliminate both errors, we proceed as follows:

(*a*) If more than 30 c. c. of the test solution are required, add half as much water as the number of c. c. of test solution is more than 30 before testing with the sodium. Thus, as 52.5 c. c. have been used, we add $\frac{22.5}{2} = 11$ c. c. of water to the mixture before testing with soda.

(*b*) If less than 30 c. c. were sufficient, then we deduct for every 5 c. c. less than 30 c. c., 0.1 c. c. from the whole quantity used. Thus, if we use 20 c. c. (10 c. c. less), we compute with 20—0.2=19.8 c. c.

2. If the urine contains 1--1.5%, NaCl, the formation of corrosive sublimate will necessitate an increased amount of the test solution, which, without being corrected, would give too great an amount of urea (15 to 25 mgr.) In order to correct this error, subtract 2 c. c. from the figures read off from the burette.

If we wish to get absolutely correct results, we must either first titrate the NaCl with a nitrate of silver solution, or use Raudenberg's method. According to this, two tests are made, for each of which 15 c. c. of mixture are prepared. The one is acidulated with nitric acid, and the mercuric nitrate solution is added until the cloudiness remains permanent. With the second test we proceed according to Liebig, with the addition of keeping the mixture neutral by means of freshly precipitated calcic carbonate. For the terminal reaction, the solution 3 (acid sodic carbonate) is employed. We now subtract the c. c. used in the first test from the number used in the second, and from this we calculate the quantity of urea.

3. If albumen is present, 20 c. c. are placed into a vessel that can be closed, a few drops of acetic acid added, and then boil until the albumen separates in coarse flakes; now close the vessel and allow to cool. Finally, filter, and proceed as before.

II. Method of Bunsen (Bunge).

Only to be used when neither sugar nor albumen are present. 50 c. c. of urine are precipitated with an ammoniacal solution of chloride of barium, filtered and 15 c. c. of this put into a tube with thick walls. Upon the bottom of the tube are 3 grammes of crystallized chloride of barium. Seal the tube and heat to 200° C. for six hours in an oil bath. After cooling, break off the point of the tube, pour the

contents upon a filter, wash out the barium carbonate that has collected, and dissolve it with sufficient quantities of hydro-chloric acid. Care must be taken to wash off and dissolve any barium carbonate that may be found adhering to the walls of the tube. All of the solution is filtered and precipitated with sulphuric acid. The precipitate of barium sulphate is collected, washed, heated and weighed.

233 grammes of barium sulphate, representing 60 grammes of urea, we can easily compute how much urea is present.

III. Method of Knop-Hüfner.

(*a*) *Solutions.*

1. *Hypobromite of sodium :* 100 grammes of sodium hydrate are dissolved in 250 c. c. of water, and mixed with 25 c. c. of bromine. Must always be prepared fresh.

2. *A saturate solution of common salt.*

(*b*) *Test.*

Dilute 10 c. c. of urine with 40 c. c. of water, fill the lower cup of Hüfner's apparatus, and also the cock, with diluted urine, fill the upper part with the hypobromite solution, and the vessel above with the salt solution, and into it put the eudiometer. After five minutes the development of gas ceases. After one hour the eudiometer is taken off, and the quantity of urea is calculated according to the method of Dumas, 1 gramme of urea producing 370 c. c. of nitrogen (at O°C and 760 m.).

IV. Estimation of Uric Acid.

To 300 c. c. of urine are added 10 c. c. of hydrochloric acid, well stirred, and allowed to stand in a cool place for 48 hours. If the urine contains albumen, this must be removed. If it contains sugar, it must be treated with mercuric acetate; the precipitate being washed upon a filter, it is mixed with a little water, then hydrogen sulphide allowed to act upon it, and again filtered. The mercuric sulphide is

washed with warm water, this water then is treated like the urine.

The crystals of uric acid are collected upon a filtering paper that has been washed with water and acetic acid, dried between two watch-glasses at 100° c. and then weighed. As the crystals of uric acid are very heavy, they can be collected by decanting the fluid; those crystals that adhere to the walls of the vessel can be removed by a feather, and will then come to the bottom.

Only when the crystals are very small does it become absolutely necessary to filter.

Uric acid is washed with distilled water until the filtrate no longer produces any reaction with nitrate of silver. It is advantageous not to use more than 30 c. c., otherwise some of the uric acid is dissolved. If more than 30 c. c. are employed, then 0.045 mgr. must be added to the whole amount of uric acid for every c. c. of urine.

Now the uric acid is dried at 100° c. between watch glasses in the air bath, dried in the dessicator, and weighed.

The difference between the two weighings represents the weight of uric acid contained in 300 c. c. of urine.

Schwanert recommends to add for every 100 c. c. of urine employed 0.0048 grammes, claiming that the result is more correct.

V. Estimation of Creatinine.

(*a*). *Reagents.*

1. *Zinc-Chloride Solution.* Pure oxide of zinc is dissolved in pure hydrochloric acid; this solution is evaporated in the water bath to the consistency of syrup (until no free acid can be detected), dissolved in strong alcohol until specific gravity of 1,200 is reached.
2. *Milk of Lime.* To be shaken before using.
3. *Dilute Solution of Calcium Chloride.*

(*b*). TEST.

200 c. c. are rendered alkaline with the milk of lime and the calcium solution added as long as a precipitate is formed. After 2 hours, filter, wash and concentrate everything having come through the paper, in the water bath, to the consistency of a thick syrup. Add, while warm, 50 c. c. of alcohol (95%), pour into a beaker and allow to stand for eight hours. Again filter and wash, and evaporate to 60 c. c.

After cooling add ½ c. c. of the chloride of zinc solution, stir with a glass rod and allow to stand for 48 hours. A compound with chloride of zinc is formed which is treated like the crystals of uric acid. In 100 parts of this compound are found 62.44 parts of Creatinine.

VI. ESTIMATION OF TOTAL NITROGEN.

The principal amount of nitrogen in urine is contained in urea, and as Liebig's method includes other nitrogenous substances, this usually suffices.

The direct method is usually performed by burning with soda-lime.

(*a*.) *Reagents.*

1. *Fresh Soda Lime.*

2. *Normal sulphuric acid*, containing 40 grammes of sulphuric acid anhydride in 1 litre of water, every c. c. corresponding to 0.014 grammes of nitrogen.

3. *Solution of Caustic Soda*, equivalent to the sulphuric acid, i. e., 10 c. c. of the one must neutralize 10 c. c. of the other.

4. *Litmus Tincture.*

(*b*). TEST.

Pour 20 c. c. of sulphuric acid into a beaker and then suck the greater part into the nitrogen apparatus of Will-Varrentrapp. Into a flask holding 100 c. c.; soda lime, to the depth of 2 c. c. and 5 c. c. of urine are put, the flask closed with a cork having two openings, and the whole placed into a sand bath. Through the one opening of the cork the connecting tube with the nitrogen apparatus passes, through the other passes a fine tube drawn out at one end and closed. Heat the sand bath as long as bubbles of gas pass through the apparatus. When this has ceased, break off the end of the fine tube and draw out

all the ammonia from the flask. Now the contents of the apparatus are poured into the beaker before mentioned; put a few drops of the litmus tincture into the fluid and add the caustic sodium solution until the red color is changed to blue.

If, by decomposition, no ammonia had been formed, we would have to have added 20 c. c. of soda to neutralize the 20 c. c. of normal sulphuric acid. If 14 c. c. only are necessary, it proves that 6 c. c. of sulphuric acid have been satisfied by the ammonia formed, 1 c. c. corresponding exactly to 0.014 grammes of nitrogen, the quantity of N. present will equal $6 \times 0.014 = 0.084$ grammes N in 5 c. c. of urine. From which the quantity passed in 24 hours can easily be found.

VII. Estimation of Albumen.

Filter the urine and take 100 c. c. (where little albumen is present), 50 c. c. (where more is present, dilute with 50 c. c. of water), or 20 c. c. (where great quantities are present dilute with 80 c. c. of water), which is to be heated for half an hour in the water bath. If the albumen does not come down in coarse flakes add 1–2 drops of acetic acid and continue to heat. Allow the fluid to pass through a weighed filter and wash with distilled water until the wash water ceases to show the Na Cl reaction with Ag No_3. The filter is then dried between watch-glasses at 100° c. and weighed.

VIII. Estimation of Sugar.

Fehling's Method.

(*a*). *Solution.*

Fehling's Solution. In 1,000 c. c. are contained 30,639 grammes cupric sulphate, 173 grammes pure, crystallized tartrate of sodium and potassium, and 500 grammes of solution of caustic soda (sp. gr. 1.12). 10 c. c. of this solution are reduced by 0.05 gr. of sugar.

(*b*). Test.

The estimation of sugar depends upon the property of

grape sugar of reducing cupric sulphate in the presence of an alkali. For this purpose urine is taken and filtered and, if the quantity of sugar present is not too small, dilute with water. Usually 10 c. c. of urine are diluted with 190 c. c. of water. With this mixture a burette is filled. A flask or porcelain dish is placed upon a wire net, and into it 10c. c of Fehling's solution diluted with 40 c. c. of water. Now heat, and, as soon as boiling takes place, add the urine drop by drop. Gradually the fluid becomes yellow, then red; finally, all the blue disappears and the red cuprous oxide precipitates very quickly. If allowed to stand for a little while the solution will be found entirely colorless, or, if too much urine has been added, slightly yellow. The entire discoloration, then, is the terminal reaction.

As this can not always be readily determined with the naked eye, it is advisable to filter a few drops into a test tube, testing one part of the fluid, having acidulated it with acetic acid, with ferro-cyanide of potassium for copper, and the other with Fehling's solution for sugar. If neither are present then the reaction has been completed.

In the estimation for sugar it is of essential importance to compute the amount of urine employed.

Supposing that we have used 25 c. c. of the urine mixture to reduce 10 c. c. of Fehling's solution. The mixture was prepared so that 200 c. c. contained only 10 c. c. of urine. In order to find out how much urine there is in 25 c. c. of the mixture we institute the proportion:

$$200 : 10 :: 25 : x. \qquad x = 1.25 \text{ c. c.}$$

1.25 c. c. of urine, therefore, was able to reduce 10 c. c. of Fehling's solution completely. But the solution is so arranged that 10 c. c. will reduce 0.05 gr. of sugar, 10 c. c. of the solution being reduced by 1.25 c. c. of urine, the latter must contain 0.05 gr. of sugar. From these data we can easily compute how much sugar is passed in 24 hours.

If albumen is present it must be removed by the method already described.

Note.—When Fehling's solution has been kept for some time it becomes self-reducing. It is, therefore, necessary before using the solution to boil it in a test tube, and if reduction does not take place it can be used for the test. By means of placing the solution in small bottles (containing about 15 c. c.) with glass stoppers, hermetically sealing and keeping them in a cool place, the solution will retain its delicate properties for years. (Tr.)

2. KNAPP'S METHOD.

(*a*) *Solution.*

10 grammes of pure mercuric cyanide are dissolved in a little water. To this is added 100 c. c. of a solution of caustic soda (sp. gr. 1.145) and the whole diluted to 1,000 c. c.; 40 c. c. of this solution reduce 100 millegrammes of sugar.

(*b*) *Test.*

Heat 40 c. c. of the solution in a beaker and add diluted urine, as in Fehling's test, until the originally-clouded mixture becomes clear and yellowish. From time to time a drop is taken out and tested with ammonium sulphide. As soon as the spot no longer shows a brown circumference the test is complete. Fehling's method and this one do not give results that correspond exactly.

The method, by fermentation, is much more laborious and not as exact as Fehling's. Very accurate results are obtained with the saccharimeter of Soleil-Ventzke or the polaris trobometer of Wild. (See Neubauer and Vogel.)

IX. ESTIMATION OF CHLORINE.

1. AFTER MOHR.

(*a*) *Reagents.*

1. *Saturated solution* of *potassic chromate.*

2. *Titrated solution* of *silver nitrate*, containing 29,075 gr. of $AgNO_3$ (18,469 gr. Ag) in a litre, so that 1 c. c. represents 10 mgr. of Na Cl (=6,065 mgr. Cl).

3. *Calcic Carbonate.*

(*b*). TEST.

10 c. c. of urine are measured into a platinum crucible; add 2 grammes of pure nitre, evaporate to dryness over a water bath, heat over a Bunsen's burner until the melted mass no longer contains any carbon. Dissolve in a little water and carefully rinse the crucible. Solution and rinsings are carefully collected in a beaker, nitric acid, free from chlorine, is then added until a weak acid solution is produced, which is then neutralized, carefully, with freshly-precipitated calcium carbonate. Without regard to the precipitate, three drops of chromate solution are added and then the silver solution is allowed to flow into the mixture. As soon as the yellowish fluid becomes reddish, it is a sign that all the common salt has been converted into chloride and that the formation of silver chromate has begun. At this moment the work is completed.

If for 10 c. c. of urine we had used 9.6 c. c. of the titrated fluid we would have 96 mgr. of NaCl present as 1 c. c. of the fluid indicates 10 mgr. NaCl.

From this we can readily determine how much NaCl present in 24 hours.

If the patient has been receiving iodine or bromine preparations, it becomes necessary to remove these from the urine. In order to carry this out, add to the solution, as it comes from the crucible, sulphuric acid, then a few drops of potassium nitrite, then shake with bisulphide of carbon, as long as this takes up I or Br, then neutralize with natrium carbonate, and proceed as above.

X. ESTIMATION OF PHOSPHORIC ACID.

(*a*) *Reagents.*

1. *Solution of Natrium Acetate.* 100 grammes of the salt dissolved in 900 c. c. distilled water and 100 c. c. of concentrated acetic acid added.

2. *Solution of uranic nitrate,* 1,000 c. c. containing 20.3 gr. pure uranic oxide. 1 c. c. represents 5 mgr. of phosphoric acid.

3. *A Solution of Potassium Ferro-cyanide.*

(*b*) *Test.*

50 c. c. of urine are measured into a beaker, mixed with 5 c. c. of the solution of sodium acetate and heated in a water bath. Then add the uranium solution as long as a precipitate continues to form. If this point cannot be determined accurately, place a few drops upon a porcelain dish, and, if upon addition of the potassium ferro-cyanide, a brownish-red boundary line is produced, cease adding the uranium solution and again heat in a water bath. See if a precipitate will now form. Usually this is not the case; then a few drops of the uranium solution are added so that the ferro-cyanide test succeeds with the boiling mixture. The border reaction then sets in, when all the phosphoric acid has been precipitated by the uranium, in that the next drop, finding no acid, is precipitated brown by the ferro-cyanide of potassium.

If we have used 13 c. c. of the solution, for instance, we could establish the following proportion (1 c. c.=5 mgr. of phosphoric acid):

$$1 : 5 :: 13 : x; \quad x=65 \text{ mgr.}$$

From which, the quantity of urine in 24 hrs. being known, the amount in 24 hours can be easily computed.

If we wish to determine the phosphoric acid that is bound to the earths; 200 c. c. of urine are precipitated with ammonia. The precipitate is collected; after 12 hours, upon a filter, washed with aqua ammoniæ (1 part in three of water), the filter perforated, and the precipitate washed into a beaker. The precipitate is then dissolved with a small quantity of acetic acid, 5 c. c. of the solution of sodium acetate added, diluted to 50 c. c. and examined as above.

The difference between the total phosphoric acid and the phosphoric acid in combination with the earths, will give the phosphoric acid united to the alkalies.

XI. Estimation of Sulphuric Acid.

100 c. c. of urine heated and precipitated with barium chloride; the barium sulphate that is formed is collected upon a filter, of known weight, washed, burnt in a crucible whose weight is also known, moistened with a few drops of sulphuric acid, and again heated. Then the whole is weighed, the difference between total weight and weight of crucible+filter, representing the weight of barium sulphate. As 34·33 parts, by weight, in 100 parts of barium sulphate, represent sulphuric acid, the latter can be easily determined.

For the exact quantitative tests, see Neubauer & Vogel, Hoppe-Seyler, etc.

CHAPTER VI.

KEY TO THE APPROXIMATE ANALYSIS OF URINE.

After having allowed the urine to stand for several hours, we first determine its physical properties:

1. The quantity in 24 hours.
2. Color and transparency.
3. Odor.
4. Reaction to litmus.
5. Specific gravity.
6. Quantity of Sediment.

If sediment has formed, the urine is poured off and examined. If very cloudy it must be filtered, and if the filtrate still is cloudy, slightly heating will clear it. The sediment is kept for further examination.

CHEMICAL EXAMINATION.

(*A*) NITRIC ACID TEST.

About 15 c. c. of clear urine are taken, and 5 c. c. of pure nitric acid are allowed to flow under it. We here find:

1. Albumen.
2. The urates.
3. Biliary coloring matters.
4. Indican.

When much iodine is present, the ring of coloring matter between the nitric acid and urine, is colored yellowish brown, and the odor of iodine is distinctly present.

Very minute quantities of these substances are only separated after some time; it is, therefore, of importance to put the vessel aside, and examine the result after a little time has elapsed. The next is the

(*B*) Test by Boiling.

Fill a test-tube one-third full with clear urine, and boil over a lamp. If turbidity is produced, there is present either albumen or the earthy phosphates. Add 1—2 drops of acetic acid; the phosphates are dissolved—not so the albumen. Now add liquor potassæ, one-half the quantity that we added of urine; albumen dissolves, but, at the same time, the earthy phosphates are brought down in the form of fine flakes. Now boil again. If the mixture becomes brown, sugar is present; if this does not occur, put the test-tube on a stand, and, after having allowed the precipitate to settle, determine its quantity and color.

In normal urine this always is white; if colored, then there may be present various coloring matters. If it appears blood-red or dichroic, then blood-coloring matter is present. In confirmation, albumen must be present and haemine crystals must be detected by the proper methods. Nearly always, blood corpuscles will be detected.

If the precipitate is pink, and the urine does not contain albumen, then vegetable coloring matter is present (especially after taking senna or rhubarb). In order to verify this, the urine must, upon addition of ammonia, become reddish, which will again disappear when acids are added.

If the precipitate is grayish, then uroërythrine, the coloring matter of fever urine, is present. This is verified by the presence of a brick-dust sediment, or the production of

a reddish or flesh colored precipitate upon the addition of a solution of plumbic acetate.

A brown color of the precipitate indicates biliary coloring matter. If the same is not decomposed, Heller's test will give a beautiful play of colors. This failing, it is decomposed; then the sulphuric acid test must be increased, the specific gravity being low, as well as a mixture of urine with a solution of caustic potash, must appear dark.

(*C*) Test for the Normal Coloring Matter of Urine.

1. Test with concentrated sulphuric acid (Heller's Urophaeïne).

2. Test for indican with concentrated hydrochloric acid and calcium chloride solution.

(*D*) Test for the Normal Inorganic Salts.

1. For the chlorides. The vessel in which the test (*A*) has been performed can be used; the two layers are stirred with a glass rod, and then 1 or 2 drops of the nitrate of silver solution are added.

2. For the *alkali* phosphates with the magnesia fluid and

3. For the *sulphates* with chloride of barium.

(*E*) Tests for Abnormal Substances.

If necessary, test for *ammonium carbonate*, *sodium carbonate*, *sulphide of hydrogen*, *leucine and tyrosine*. These can be determined by the preceding tests.

(*F*) Examination of the Sediment.

First determine color and consistency of the sediment (whether crystalline, a powder, flaky, etc.); then its composition. This can be done either chemically or, better, mi-

crochemically and microscopically. Finally, we determine the organized admixtures (epithelium, casts, spermatozoa, etc.)

Having examined an urine according to this method, it is of importance, especially for the beginner, that all the results are noted in a brief and schematic way so that an oversight can be had and the result easily deduced.

The following method can be used to great advantage:

Physical Properties.
Normal Substances.
H_2SO_4 Test. Cl.
Ind. " Eph.
$\overset{+}{U}$. Aph.
$\overline{U}$. Sph.
Abnormal Substances in Solution.
Sediment.
Result.

Divide a sheet of paper into four parts; the upper for the enumeration of the physical properties, the second for the quantity of normal constituents present. The abbreviations employed are as follows:

H_2SO_4 test = Sulphuric acid test for coloring matter.
Ind. = Indican.
$\overset{+}{U}$. = Urea.
$\overset{-}{U}$. = Uric acid.
Cl. = Chlorides.
Eph. = Earthy phosphates.
Aph. = Alkaline phosphates.
Sph. = Sulphates.

In order to express whether a substance is present in normal, greater or smaller quantity, the following are employed: For an increase the sign +; for diminution the sign —; for normal the letter "n". A great increase or diminution are represented by "gr.+" and "gr.—;" also, a moderate increase or diminution by "m+" and "m—."

The third division is for the abnormal substance found in solution.

The last for the description of the sediment and the result, the diagnosis. A sheet of paper filled out looks like the following:

PHYSICAL PROPERTIES.

Quantity = 4,000 c. c.
Pale yellow, somewhat cloudy, acid.
Sp. gr. = 1,040; Slight sediment.

H_2SO_4 test - - gr.— Cl. - m—
Ind. - - - - - m.+ Eph. - gr.—
$\overset{+}{U}$. } - - - - m.— Aph. } m.—
$\bar{U}$. } Sph. }

ABNORMAL SUBSTANCES IN SOLUTION.

Sugar in large quantities.

SEDIMENT.

Consists of mucus in normal quantity.
Microscopically a few yeast fungi are detected.

RESULT:—Diabetes Mellitus.

Using a blank like the above will facilitate, not only the analysis but also the diagnosis. Coming back to the above we deduce as follows:

1. From the quantity in 24 hours; *Polyuria.*

2. From the specific gravity, and the amount of solids found by computation from it; *Diabetes.*

3. From the pale color and the absence of the urates; *the absence of fever.*

4. Finally, from the presence of sugar; *Diabetes mellitus.*

CHAPTER VII.

General Diagnosis.

At a time when the examination of urine consisted solely of a prejudiced observation of physical properties; when the so-called "urine signs" were forced into a system the result of dreams, it was impossible for the examination of urine to be an aid to the discovery of pathological processes, it frequently serving to cover over ignorance and quackery.

It is only since organic chemistry and microscopy have progressed; since the connection between the composition of urine and the changes in the economy, on the one hand, and the structure of the urinary apparatus on the other, have been thoroughly recognized, that the analysis of urine can be termed a scientific procedure. No one doubts, at the present time, but that it is of great value in the diagnosis of disease, in some cases it alone giving us an insight into the stage, the nature and intensity of the disease.. We would err if we would consider ourselves capable of diagnosticating all forms of disease from the urine, but it seems equally unjustifiable to neglect this branch entirely.

Before proceeding to the diagnosis of the diseases of the urinary organs we will mention the important general rules.

We take up that order which is of greatest importance to the practicing physician.

1. Measure the quantity of urine passed in 24 hours and determine whether normal, increased or diminished. The *normal quantity* is, about, 1,500 c. c.; if the quantity is very much above this, we have *polyuria;* if very much below, *oliguria*, and, if no urine whatsoever is passed, *anuria.*

Polyuria may be *physiological* or *pathological.* In the former instance it is *urina potus* or *urina spastica*, and in the latter, *hydruria* or *diabetes.* In order to make this differential diagnosis we compute the amount of solids in 24 hours, by *Trapp's* or *Haeser's* coëfficient. If this amount is nearly normal (70 gr.), then we have an *urina potus*, *i. e.*, an urine with normal solids that has been diluted. If the solids are diminished, then it is *hydruria*, as observed in many cachexias. If the solids are very much increased, then we have *diabetes;* —sugar being detected, in appreciable quantity, in the latter instance, it is *diabetes mellitus*, no sugar being present, *diabetes insipidus*, (when the nitrogenous substances are increased, *azoturia*).

Oliguria can be readily diagnosticated and occurs principally in febrile diseases. The urine usually is dark and very much concentrated. In the last stages of disease of the kidney, when uræmia sets in, the quantity of urine is always diminished. A mild form of oliguria may also be congenital; temporarily it is produced by the abstraction of water, after profuse sweats or after diarrhœa.

Anuria, the uretha being pervious, can only occur in grave

disorders of the kidney with uræmia; at other times it is found in strictures, calculi and neoplasms as so-called *retention of urine.*

Having satisfied ourselves regarding the quantity, we seek to determine whether.

2. The urine is indicative of a febrile state or not. From this we can frequently see if the process is acute or chronic, the former usually being accompanied by higher degrees of fever.

The urine of *fever* is usually dark, reddish-yellow, concentrated and diminished in volume. If the quantity is not diminished, rather increased; occurring very rarely, the coloring matter of urine will, nevertheless, be found increased. With the nitric acid test a distinct layer of urates can always be detected.

If an acute exudative process is present, then, in the stage of exudation, the urine is concentrated, acid, containes many urates, that come down, when cold, in the form of brick-dust sediment. At the same time urea, the sulphates and the alkaline phosphates are increased; the chlorides, on the other hand, diminished. With the increase of disease the chlorides diminish and may be entirely absent.

In the stage of absorption the concentration of the urine gradually dimishes, the reaction becomes neutral or alkaline (ammonium carbonate); the chlorides are again present in normal quantity and in the sediment are found urates (in the form of urate of ammonia) and the earthy phosphates. At the same time the quantity of urine may be normal or even diminished.

We can readily diagnosticate the *febrile state*, but can not

diagnosticate the form of fever (except febrile diseases of the urinary apparatus). Even in diseases of the kidneys we may err in that we may take an accompanying disease to be the principal affection. We examine, for instance, the urine of scarlatina. We find a febrile state, in addition, however, a desquamative or parenchymatous nephritis. As a result of the uroscopic developments we can only diagnosticate an acute nephritis, which evidently only accompanies the scarlatina, the latter not being detected by the analysis.

Differential diagnosis between the different forms of fever, then, is impossible; but, nevertheless, we ought to examine the urine, as from it we can discover increase or diminution in the process, or other complications. The reappearance of the chlorides, for example, is considered a favorable sign, their disappearance or the appearance of albumen an unfavorable one.

Among the febrile processes there are some that require mention on account of their giving to the urine certain characteristic properties.

We find:

In jaundice, constituents of bile always present in the urine.

In jaundice that is mild (*icterus levis*), produced by absorption of bile, we find only a febrile state, and a goodly quantity of biliary coloring matter; the chlorides are sometimes diminished.

In severer forms of jaundice produced by disease of the liver (*icterus gravis*), we find, besides great quantities of *urates* and *biliary coloring matter*, albumen and, sometimes, small quantities of *biliary* acid. The *chlorides* are usually absent.

In *acute yellow atrophy* of the liver we usually find an urine rich in biliary coloring matter, having a low sp. gr. and acid

reaction. Urea is much diminished and, in its stead, we find *leucine* and *tyrosine*. The chlorides disappear, besides, the urates and albumen are present, the latter in abundance. Even biliary acid may be detected in this urine. In the sediment are found great numbers of epithelial tubes and fibrine casts; in addition, epithelium from the kidney and blood corpuscles.

In *acute pulmonary affections* we find a great quantity of urates. In diseases of the heart or irregularities in circulation, we find stasis in the venous system and, as a result, albuminuria (hyperæmic kidney). In *peritonitis*, we usually find large quantities of indican (Senator).

The urine of meningitis is usually very much concentrated, corresponding to the slowness of the pulse. As the differential diagnosis between typhus and meningitis is very difficult, frequently impossible clinically, the urine has been looked to for assistance. Unfortunately this can not be relied upon. It is said that the urine of meningitis has a high specific gravity, a faintly acid reaction and contains an increased amount of urates besides a small quantity of albumen. In addition, it is claimed that when the urine of this disease is boiled, the earthy phosphates are precipitated without the addition of an alkali; the chlorides are not very much diminished. For typhus the urine is described as having a lower specific gravity, acid reaction and no spontaneous precipitation of phosphates; the chlorides are always much diminished. The urates are present; albumen may also be found in considerable quantity. At the same time, however, the urine of typhus is said to have large quantities of ammonium carbonate in solution, although the reaction is acid. In meningitis spinalis much indican has been found.

In contradistinction to meningitis cerebralis, the sp. gr. is said to be diminished (Heller).

In *acute articular rheumatism*, in addition to high specific gravity, acid reaction, increase in urea and in urates, a great increase in the earthy phosphates is claimed as characteristic. The sediment contains pink urates and calcium oxalate colored by uroërythrine. If pericarditis sets in, the chlorides and earthy phosphates are rapidly diminished, but the uroërythrine becomes even better marked than before.

If the urine is not colored dark yellowish red and does not contain urates in large quantity, then we can assume that the disease is not accompanied with fever. For a few of those diseases that are without fever, therefore principally chronic, characteristic properties of the urine have been described which are enumerated on account of completeness.

Chlorosis furnishes a very pale urine, of low sp. gr. corresponding with the diminished waste of tissue in the body. In hysteria the urine is similar, but the quantity is sometimes, and indican is always, increased (*urina spastica*.) Very pale urine is found, also, in hydruria and diabetes. In diabetes mellitus the sp gr. is increased; usually there is found an increase in indican, and in the late stages of the disease, albumen is present. The other normal constituents are diminished in per centage but increased absolutely (with the exception of uric acid). In diabetic urine handsome yeast fungi, as well as networks of penicillium, are frequently found.

In *chronic diseases* of the *spinal cord* there occurs frequently a pale and light urine, which, in addition to much indican, and sometimes albumen, is said to contain sugar. (?) Heller states that in the sediment he has frequently observed sarcina.

In *rickets* and *malacosteon* the earthy phosphates are very much increased, so that they form a heavy deposit.

In *diseases* of the *bones*, when they affect any great amount of osseous substance, the calcium salts are frequently found increased in the urine, in the form of the oxalate as well as the earthy phosphates, both in solution and in the sediment.

A very acid and concentrated urine is found in *chronic rheumatic arthritis*, depositing a copious sediment of urates and oxalate of lime. A decided increase in earthy phosphates is claimed as characteristic.

In *gout* the urine is similar to that of the above, only that uric acid is diminished in the urine and deposited in internal organs. Occasionally, however, a beautiful deposit of free uric acid is found.

In *intermittens*, during the chill, the urine is increased, pale and transparent; whilst it is dark during the period of fever.

In *chronic diseases of the liver*, notwithstanding the absence of fever, we find a dark, acid and concentrated urine. Biliary coloring matter that is not decomposed is rarely present. But we find the tests for normal coloring matter much increased—usually uroërythrine is present. The increase in these coloring matters is said to depend upon the presence of decomposed biliary coloring matter and increase in their excretion. The earthy phosphates are commonly diminished. In the sediment are found urates, and sometimes oxalate of calcium, both colored by uroërythrine. In *skin diseases* of a chronic nature, and especially in those in which a great area of skin becomes disabled for perspiration, we frequently find kidney disease as a complication, for instance, pemphigus, etc.

In *scorbutus* and *purpura haemorrhagica* hemorrhages from the kidney are not uncommon. Also in *melanaemia*, where parenchymatous diseases of the kidney are found in addition.

In *leucaemia* the urine is loaded with uric acid, lactic and hippuric acids also occurring.

CHAPTER VIII.

Diagnosis of Diseases of the Urinary Apparatus.

If we can prove the presence of albumen in urine that does not contain pus, blood or any other albuminous fluid, then we have before us a case of *true albuminuria*. We are then dealing with a disease of the kidney. If blood and pus are present in large quantities, and albumen in corresponding quantity, then we have a case of *false albuminuria*, due to disease of the pelvis, the ureters or the bladder. If pus or blood are present and great quantities of albumen are detected, then we are dealing with *mixed albuminuria* (Vogel).

Great practice alone capacitates for determining whether albumen is present in sufficiently large quantity to constitute mixed albuminuria. This can be acquired by means of mixing with normal urine pus from wounds and then testing for albumen.

Microscopic and Chemical Aids for the Diagnosis of Various Forms of Albuminuria.

(*a*) true albuminuria.

1. *Hyperaemia of the Kidney.*

In active hyperaemia, depending upon the imbibition of

much fluid, no albumen is found. The quantity in 24 hours is very much increased; color of the urine, pale yellow, even watery, the sp. gr. very low. Normal constituents are usually increased.

It is only when the kidneys have been over-exerted for some time, as in diabetes, that we find albumen present in small quantity. In the same way albumen is found in hyperaemic conditions of the kidney ($\frac{1}{10}\%$, usually less) that are caused by irritating substances excreted by the kidneys. For example, after the continued administration of balsam copaibæ, turpentine, cubebs, corrosive sublimate and other acrid remedies.

The chemical composition of the urine must also be considered as cause for an irritated condition; *i. e.*, hyperaemia of the kidneys. It is well known that urine very much concentrated, or very acid, can cause the most varied symptoms. Occasionally, mostly transient, albumen is found in such urine.

In oxaluria and the presence of large quantities of uric acid, partly on account of mechanical, partly chemical, irritation, especially when the urine is very acid and the crystals of uric acid are lance-shaped, albumen can be detected in small quantity. In these cases it usually disappears upon the internal administration of alkalies, excellent solvents for urates and oxalates. This form is not infrequently the first beginning of calculus of the kidney.

A transitory presence of albumen, in small quantities, is detected after convulsions, epileptic attacks, attacks of chills and fever, and in various forms of spasms of the blood vessels; frequently in acute febrile diseases (febrile albuminuria of Bartels), especially in the acute exanthemata, not infre-

quently in other inflammatory affections of the skin, anthrax, furunculosis, erysipelas, after burns, etc. Not uncommonly in hyperaemia, there is begun a parenchymatous affection if the cause continues to act.

In passive hyperaemia, occurring as a result of stasis in the venous circulation, the albumen increases and diminishes with increase or diminution of pressure.

This form of kidney is most commonly found in valvular lesions of the heart that have not been compensated. Regulating the circulation by proper remedies causes the albumen to disappear. The hyperaemic kidney is also found in chronic diseases of the lungs, notably in emphysema; furthermore in tumors and exudations that prevent the flowing back of the venous blood; for example, large pleuritic exudations, ascites, ovarian tumors and pregnancy. In puerperal convulsions we do not always find the hyperaemic kidney (Rosenstein), but very frequently parenchymatous nephritis (Bartels).

As a result of marasmus and cachexia we also find this form of disease.

The urine, in simple hyperaemia of the kidney, is as follows: sp. gr. increased, but not always; the quantity either diminished or normal; reaction acid.

Albumen present in small quantity ($\frac{1}{10}\%$ and below).

In the sediment are found either no organized elements or blood corpuscles and epithelia from the straight uriniferous tubules. Hyaline casts hardly ever occur.

In febrile albuminuria the quantity of urates is increased, and that of the chlorides very much diminished.

In the hyperaemic kidney proper (stasis,) the quantity is always diminished, sp. gr. high, color dark,and the reaction acid.

The urine contains a great quantity of urates that frequently cause the urine to become cloudy and form a large deposit.

Albumen is present $\frac{1}{5}$ % and above.

In the sediment are found hyaline casts and kidney epithelium.

This form can be differentiated from parenchymatous nephritis by the absence of cellular elements (blood, lymph corpuscles and granular epithelium of the kidney) and granular casts in the sediment.

From chronic interstitial nephritis and the amyloid kidney, by the dark color of the urine, its high sp. gr., its diminished quantity and richness in urates.

Parenchymatous Nephritis.

There are two forms of parenchymatous nephritis: acute and chronic. The acute form is rarely primary, but developed from some other disease; the chronic is usually primary, and forms the second stage of what is called Bright's disease by the authors.

(*a*) Acute Parenchymatous Nephritis.

Again, a subdivision can be made, a mild form, so-called catarrh of the uriniferous tubules or desquamative nephritis, and the real acute parenchymatous (diffuse or croupous) nephritis, the so-called acute Bright's disease.

(α) Catarrh of the Uriniferous Tubules, or Desquamative Nephritis.

Attacks principally the straight uriniferous tubules. The disease lasts from 8 to 14 days, frequently less. The patients have little fever; they complain of pain in the limbs,

weakness and pains in the back. Frequently the disease runs its course without compelling the patient to seek his bed. We rarely find œdema.

The urine presents the following changes:

The quantity is either normal or slightly diminished, the same is true of the sp. gr. The color of the urine is wine yellow, rarely yellow; the reaction acid. It is always cloudy from admixture of cellular elements and frequently deposits a dense sediment.

The normal constituents are unaltered. Of abnormal substances albumen is found in $\frac{1}{10} - \frac{1}{5}$ %, and traces of blood coloring matter.

The sediment is principally made up of an increased mucous secretion. With the microscope we find numerous epithelial cells from the straight tubules, usually little altered, sometimes colored brownish by the blood coloring matter.

They are frequently adherent to each other, forming the epithelial tubes or stick to hyaline casts forming epithelial casts. Besides, are found single hyaline casts, red blood corpuscles and lymph corpuscles in great number.

This form develops as a morbid reaction after the introduction of instruments into the bladder, after catheterisation of a sensitive bladder, the dilatation of strictures, lithotripsy, etc. In addition to this, after acute inflammatory processes, especially upon the skin, the exanthemata. It may also develop ex-contiguo from acute cystitis after gonorrhœa.

(β) Acute Parenchymatous Nephritis Proper.

This process may be ushered in by very turbulent symptoms, or may occur without marked subjective symptoms, the latter occurring in cachectic, reduced individuals.

Dropsy is the first symptom that causes uneasiness to

patient and physician. It appears as the characteristic œdema of the eyelids and face. Severe cases are accompanied by anuria and convulsions. The smaller the quantity of urine in 24 hours, the more intense is the attack, so that anuria lasting for some time nearly always results fatally.

We find the following in the urine:

The quantity is very much diminished, sometimes to 250 c. c. Sp. gr. is usually increased, the reaction acid, the color brownish yellow and very turbid, frequently having a large deposit of cellular elements.

The normal constituents are diminished.

Of abnormal substances we find large quantities of serum-albumen and blood-coloring matter. The quantity of the former varying from 1, 5 to 6 per cent., so that the urine solidifies upon boiling.

The sediment is usually of a brownish color and consists, principally, of coarse, sometimes long or spiral, casts of fibrine, colored by the blood coloring matter. These sometimes contain a great number of white or red blood corpuscles (blood casts,) or brown epithelial cells of the uriniferous tubules (hemorrhagic). In other cases only débris of cells is found, surrounding the nuclei and adhering to or imbedded in the substance of the casts. In addition, we find cells from the tubules, many blood and lymph corpuscles and much detritus colored brown by the blood coloring matter.

This form is either a primary disease or a sequela to another acute disease. It is very frequent after the acute exanthemata, especially after scarlatina; then after diphtheria, relapsing fever, phlegmonous inflammations, erysipelas and carbuncles; after the administration of preparations made from cantharides (cantharidin), as well as after the internal

use of caustic remedies (corrosive sublimate). It is frequently observed after catching cold and after burns. After inflammatory rheumatism, cholera and during pregnancy it is not uncommon.

This form also develops during the course of chronic parenchymatous nephritis.

The prognosis is usually favorable but death may ensue from acute uraema or the form may be changed to a chronic inflammation.

(γ) Chronic Parenchymatous Nephritis.

In this form also, the first symptom is dropsy. Fever is absent.

The urine shows the following changes.

As long as the disease continues to progress, and during its acme, the quantity is diminished; as soon as the inflammation recedes, the quantity increases and in the stage of atrophy may be very much increased. Its color is yellowish, often brownish yellow, turbid with cellular elements, forming an appreciable sediment. The reaction is acid and the sp. gr. usually diminished.

Normal constituents, especially urea, are frequently diminished.

Albumen is found in considerable quantity, (½ to 1 to 2 %) and blood coloring matter can be, commonly, detected.

In the sediment are found dark, granular casts, also half granular casts, *i. e.*, those that are granular in spots, the rest of the cast being made up of hyaline substance. There is also found granular epithelium of the kidney, red and white blood corpuscles and molecular detritus.

In the stage of secondary atrophy, the quantity is very much increased, the sp. gr. very much diminished, the color

pale yellow, the urine turbid and having an appreciable sediment. When the atrophy affects boths kidneys, the excretion of normal constituents, especially of urea, is very much diminished. Albumen is present in small quantity, $\frac{1}{10}$ to $\frac{1}{5}$ %. In the sediment are found granular masses of detritus, granular epithelium of the kidney and fragments of granular casts.

In the minority of cases does this form arise from the acute form, generally it runs its course insidiously. Most frequently it arises from the acute form after scarlatina, and rheumatic processes, after profuse suppuration in the bones and also from the nephritis of pregnancy.

The form that is chronic from the beginning, frequently develops from purulent processes in bone and the joints, as a result of syphilis, phthisis, malaria, scrofulosis and cachexia. Intemperance is also considered as cause.

The prognosis is not very favorable. Cases occur in which, after dropsy and albuminuria has lasted for years, health is regained; but these are exceptions. After syphilis and malaria, as well as after osseous suppuration, a cure can sometimes be affected by the proper remedies.

5. Interstitial Nephritis.

The small amount of interstitial connective tissue present in the kidney may be subjected to hyperplastic proliferation or to destruction by suppuration. As a result we have two forms of interstitial nephritis: the hyperplastic and the purulent.

(*a*) Hyperplastic Interstitial Nephritis—Cirrhosis of the Kidney—Contracted Kidney Proper.

This disease rarely occurs in the young, most commonly in the old.

It may exist for a long time and have developed fully without calling attention to its existence by symptoms. Dropsy rarely sets in and when it does, only in the last stage.

A bounding pulse of high tension, as well as enlargement of the left ventricle of the heart are the usual symptoms of this form of kidney disease.

Disturbance of sight is the most common complication of this disease, frequently being the first symptom that forces the patient to seek help.

In the urine we find as follows:

Its external appearance is that of a normal urine; clear, transparent, of a wine-yellow color. Its quantity is usually increased, but polyuria is not always the rule. The sp. gr. is either normal, or, more commonly, reduced; the reaction is acid.

The normal constituents are unaltered, as a rule.

Albumen is found in moderate quantity ($\frac{1}{10}$ — ½ %). It may disappear entirely — occurring especially when the patient is in bed, so that we find much less albumen in the morning urine than in that passed during the day.

Macroscopically no sediment can be observed. Even with the microscope we frequently fail in finding anything abnormal. Only after careful and repeated examinations do we find a single hyaline cast, a blood corpuscle or epithelium from the kidney.

The prognosis, when the diagnosis has been established, is usually unfavorable, but the course may be very long.

The etiology is, as yet, dark.

(*b*) Suppurative Interstitial Nephritis.

This form may be of traumatic, idiopathic, pyaemic or

metastatic origin. Frequently it originates in chronic pyelitis, in that the disease of the pelvis spreads to the connective tissue of the kidney and causes suppuration. This form is the usual termination of cases, in which surgical interference with the urinary organs has been had. For instance, after catheterisation of a paralytic bladder, after forcible dilatation of strictures, after lithotripsy, suppurative nephritis sets in.

To this form, therefore, the name of "the surgical kidney" was formerly given.

Calculus of the kidney predisposes to this form, complicated by large abscesses of the kidney and pyonephrosis.

We find the urine of the following description:

Its color is yellow; it is turbid and scanty; its smell is frequently fecal; sp. gr. diminished, and reaction either neutral or alkaline.

The normal constituents, especially urea, are diminished.

Albumen is present in considerable quantity (½ to 1%). Blood coloring matter is also present; not infrequently we find large quantities of carbonate and sulphide of ammonium.

The sediment is copious and consists, principally, of pus, mixed with blood in greater or less quantity. Microscopically are found numerous bacteria, molecular detritus, epithelia from the kidney, and thick, dentritic casts made up of bacteria (*Pyelo-nephritis parasitica*—Klebs).

If complicated by parenchymatous nephritis we also find dark, granular, thick casts coming from the straight uriniferous tubules.

The course of the disease is usually acute, and the termination death. In chronic cases the larger abscesses break into the pelvis.

Kidney abscesses can only be diagnosticated by means of

determining the quantity of pus discharged—easily accomplished by collecting the urine in appropriate vessels. Pus appearing and disappearing suddenly, with the microscopic signs of necrotic kidney-tissue (glomeruli, uriniferous tubules) are the best indications for the existence of an abscess.

4.—The Amyloid Kidney.

Amyloid degeneration of the kidney is usually a symptom of a constitutional disorder. It occurs in profuse suppuration of bone, as well as in other suppurative processes that last for a considerable length of time. In pyonephrosis of one side the other kidney, frequently becomes amyloid. Scrofulosis, chronic tuberculosis, syphilis and malaria, favor the development of this form of disease. Occasionally it is found idiopathically. Amyloid kidney complicated by parenchymatous nephritis is of frequent occurrence.

This degeneration develops without producing any important symptoms; but this rule can be laid down that an amyloid kidney always secretes more urine, in 24 hours, than a normal kidney. The quantity, however, never becomes so great as in atrophy of the kidney.

The urine is pale yellow, clear, and has a low sp. gr., an acid reaction and is without a macroscopic sediment.

The normal constituents are usually diminished.

Serum-albumen is constantly found in moderate quantity (from $\frac{1}{10}$ to 1 or 2%). In addition there is found a considerable amount of globuline (Senator, Edlefsen) which may be considered as characteristic of this form of disease.

In the sediment, frequently, no cellular elements are found, sometimes, delicate hyaline or waxy, shining, yellow-

ish casts. More rarely amyloid epithelium of the kidney is observed, which, in common with the casts, changes to a mahogany color upon the addition of an aqueous solution of iodine and upon the further addition of sulphuric acid becomes violet. In the uncomplicated amyloid kidney, blood is not found in the sediment.

The prognosis depends upon the disease at the bottom of the kidney disease. In syphilis and malaria we will, therefore, have the best results.

In the differential diagnc is of the various forms of true albuminuria, the following additional points must be taken into consideration.

1. If we find a sediment that can be detected with the microscope, that is made up of cellular elements, (blood, pus corpuscles, casts, etc.,) we have either a parenchymatous nephritis or an interstitial suppurative nephritis.

a. In parenchymatous nephritis we find epithelial, fibrine and granular casts, kidney epithelium, blood, and lymph-corpuscles.

b. In suppurative interstitial nephritis we find pus, and blood corpuscles, bacteria, sometimes casts of bacteria, or short and thick, dark, granular casts.

2. If the urine is clear, or cloudy with urates, and we find no sediment of cellular elements then we either have an hyperæmic kidney, an hyperplastic interstitial nephritis, or an amyloid kidney.

a The hyperæmic kidney can be differentiated from the other two; by the diminished quantity of urine; by its dark color, its high sp. gr., and frequently by the abundance of urates it contains.

b The amyloid kidney by its having globuline, and waxy

casts, and amyloid kidney epithelium. Clinically we find in amyloid degeneration (as well as in parenchymatous nephritis) dropsy, while in true atrophy this is the exception, and then occurs late in the disease.

c In true atrophy we find hypertrophy of the heart and a bounding pulse, neither occuring in the parenchymatous nephritis and amyloid kidney. In the amyloid kidney we find enlargement of the liver and spleen (amyloid degeneration).

(*B*) Forms of Mixed Albuminuria.

Mixed albuminuria is characterized by the urine always containing more albumen than corresponds with the quantity of pus present in the sediment. It includes those diseases of the pelvis of the kidney, which, when advanced, also attack the kidney, complicating pyorrhœa with true albuminaria.

As a proof that the papillary portion of the kidney is also affected in the pyelitic process, we refer to the occurrence of kidney epithelium in the sediment. We also find, when the process has continued for some time, that the pelvis is dilated at the cost of the papillary portion, the latter being more or less consumed.

1. Pyelitis.

Pyelitis frequently accompanies acute febrile diseases, also parenchymatous nephritis and (in the later stages), diabetes mellitus. The use of cubebs, copaiva, etc., is also sometimes followed by this form of disease. Renal calculi, parasites, tumors and tuberculosis in the pelvis are nearly universally accompanied by pyelitis. Ex contiguo, it or pyelo-nephritis develops from stasis of urine, as we find it in hypertrophy

of the prostate, paralysis of the bladder, strictures of the urethra, etc. Pyelitis is also produced by compression of the ureters by tumors, exudations, the retroflexed or gravid uterus; as well as after gonorrhœa, mechanical irritations of the neck of the bladder and of the bladder itself, by surgical instruments, etc.

We can distinguish two forms of pyelitis; the acute and the chronic. Besides, we frequently have points offered us for the diagnosis of pyelitis calculosa and tuberculosa in the sediment.

Croupous and diptheritic pyelitis are usually caused by such grave diseases that the latter cover over the symptoms of pyelitis.

(*a*) Acute Pyelitis.

The best type is found after surgical interference with the urinary organs; in the course of acute inflammatory affections and after gonorrhœa.

The quantity of urine is diminished moderately, the urine is dark, cloudy, has a high sp. gr. and acid reaction. Upon allowing to stand an appreciable deposit is found.

Normal constituents are unchanged unless fever be present, then an increase in the urates and a diminution in the chlorides is observed.

Albumen is always found in greater quantity than would correspond with the comparatively, small sediment of pus ($\frac{1}{10}$ — ½%). Blood coloring matter is not constant and, when present, only in small quantity.

The sediment is principally made up of mucus, mixed with more or less pus. The pus cells are round, frequently many united to form an oval or cylindrical plug. These

come from the papillæ and frequently contain epithelium. We always find blood corpuscles: epithelium from the papillary portion of the kidney, of an ovoid or pear-shape form, is found in great abundance. Frequently two or three epithelial cells still adhere. Sometimes we find the epithelial cells tinged by blood coloring matter.

Epithelial cells with one or two processes, arranged like shingles, usually called epithelium from the pelvis, is not at all characteristic for pyelitis. Indeed, this epithelium from the pelvis can hardly be distinguished from that of the bladder. Besides, these cells are not always found in pyelitis, therefore the epithelium from the papillary portion of the kidney alone is characteristic for this form of inflammation.

In acute pyelitis, epithelium from the kidney is always found in great abundance (10 cells and over in one field); in chronic pyelitis, on the other hand, it is not very abundant.

Acute pyelitis, when the result of surgical interference, of acute inflammatory processes or gonorrhœa, usually allows of a favorable prognosis, in that a few weeks are sufficient to affect a cure. Sometimes the acute form becomes

(*b*) Chronic Pyelitis.

In chronic pyelitis the quantity of urine passed in 24 hrs. is always increased, so that polyuria may be put down as a characteristic sign of this disease. In severe cases, the quantity averages from 5 to 6 litres. The color of the turbid urine is pale reddish-yellow, sometimes a slight greenish shade. The sp. gr. is always diminished and the reaction acid. The deposit corresponds with the amount of pus present.

Albumen is always found in larger quantity than could be

expected from the amount of pus present ($\frac{1}{10}$ — ½ %). Blood-coloring matter is not always present.

The sediment has a greenish-yellow color; is flaky, does not adhere to the vessel, and is made up of pus, principally. Not infrequently, the pus cells are forked and branched, in contradistinction with other purulent processes in the urinary organs. They also form round, oval or long plugs (from the ductus papillaris) that are characteristic of chronic pyelitis.

Epithelia are found in small number, and when suppuration is profuse they are entirely absent, probably on account of their becoming pus cells by endogenous growth.

Blood corpuscles are not found in the ordinary chronic pyelitis, but when this is the result of renal calculi, tuberculosis, tumors, or entozoa, they are never absent.

The prognosis is rarely a favorable one. With us, it is usually a complication with the formation of calculi. The termination in pyonephrosis, then perinephritis, and escape of the pus externally, more rarely into the intestine or bladder, is not uncommon, usually occurring in young or healthy individuals. In weak patients the pyelitis becomes interstitial nephritis finally terminating in chronic uræmia.

(*C*) Pyelitis Calculosa.

Renal calculi are formed, principally, by the deposit of uric acid in the kidney or pelvis, and therefore those stones that pass spontaneously are of a yellowish brown color, and made up of uric acid or urates. In addition, we have cystine (very rare) and the so-called secondary formation; after-hemorrhage or long-continued suppuration, by the deposit of the earthy phosphates, as the origin of renal calculi. Oxalate

of calcium, very rarely is the primary deposit, but frequently forms layers.

The most common cause for the formation of renal calculi is the deposit of uric acid, on account of its absolute or comparative excess. This is favored by the acidity of the urine, increasing with its concentration, producing those rough crystals of uric acid which nearly always form the nucleus of these calculi. The predisposition to calculi is to be sought for in concentrated, highly acid urine, rich in uric acid, especially when it crystallizes in the rough or lance-shaped crystals.

The beginning of this disease can be diagnosticated when, besides the properties of the urine already enumerated, we find mild albuminuria (hyperæmia of the kidney) and single blood corpuscles in the sediment. The albuminuria is only temporary, and appears when the urine is either very much concentrated or contains very much uric acid in excess.

The presence of large concretions can be diagnosticated by the occurrence of parenchymatous hemorrhages. The urine is reddish brown or coffee colored, especially after bodily exercise.

If the calculi are not passed then there arises pyelitis—*pyelitis calculosa.*

This may be found either in a mild or severe form.

The mild form occurs with calculi of small diameters, and frequently has characteristic elements in the sediment; whilst the severe form can only be differentiated from chronic pyelitis by the presence of blood corpuscles in the sediment. The latter form is usually observed with large calculi, forming a focus for pyonephrosis, paranephritis and emptying of the pus.

The milder form shows the following changes in the urine:

The quantity of urine is usually normal, sometimes diminished, never increased. The color is dark, its sp. gr. normal or increased, reaction very acid, the urine frequently having a considerable sediment.

Uric acid is present in excess (uric acid present in the sediment, and the detection of a layer of urates with the nitric acid test).

Albumen is found in from $\frac{1}{10}$ to $\frac{1}{2}\%$, always a greater quantity than would correspond with the amount of pus present. Blood-coloring matter is always present, if only in small quantities.

The sediment is made up, principally, of lance-shaped uric acid crystals (cystine, oxalate of lime), mixed with curdled pus. Besides, we find numerous red blood corpuscles (especially microcytes) and epithelia from the kidney.

The diagnosis is made positive by the clinical signs and by the absence of calculi upon sounding the bladder.

Renal calculi only when small offer a favorable prognosis. When these are large or branched the prognosis is always unfavorable, or at least doubtful. The greater the suppuration and the longer it lasts the more unfavorable does the prognosis become.

The disease is usually unilateral.

(*D*) Pyelitis Tuberculosa.

As a rule, pyelitis tuberculosa is a symptom of general tuberculosis or tuberculosis of the uro-genital apparatus. For this reason we frequently find it complicated by chronic parenchymatous affections of the kidney (nephrophthisis—nephritis ulcerosa). In those cases in which tuberculosis of the

pelvis and kidney, both, exist, we find large, waxy casts, much molecular detritus, pus and blood corpuscles and kidney epithelium in the sediment. A great quantity of albumen is found in the urine.

Simple pyelitis tuberculosa, on the other hand, produces the following changes:

The quantity of urine is not increased very much; its color is yellow, frequently brownish red (on account of the admixture of blood). It is always cloudy, has a normal or diminished sp. gr. and an acid reaction. The sediment is grayish or brownish, and flocculent.

The excretion of the normal constituents is not very much changed.

Albumen is found in from $\frac{1}{10}$ to $\frac{1}{2}\%$. Blood-coloring matter can always be detected.

The sediment consists of pus, principally, and a small quantity of blood; in addition, we find kidney epithelia and molecular detritus, mixed with bacteria, the latter united so as to form spherical or cylindrical bodies.

The presence of blood corpuscles, usually denotes an ulcerative process in the pelvis, and will, therefore, be observed both in the urine passed during the day and during the night; in pyelitis calculosa, on the other hand, the urine passed in the morning, or whilst the patient is at rest, contains much less blood than that passed during the day or after exercise. In tubercular pyelitis the desire to pass water is not accompanied with as much pain and is not so frequent as in calculous pyelitis. In addition, the usual symptoms of lithiasis are absent.

The diagnosis is much easier if we find hard, plastic exudations in the testicles, scrofulous cicatrices, enlargement of

glands, or other diseased processes in bone, deep fistulæ in ano, etc.

When general tuberculosis is present, the prognosis is always unfavorable. In tuberculosis of the genital organs, when affecting young and healthy individuals, improvement or comparative health may be secured, as after the removal of a tubercular testicle, for example.

In *echinococci* we sometimes find pyelitis, which cannot, however, be distinguished from any ordinary pyelitis. It is only when the tumor has emptied into the pelvis that we find the characteristic cysts in the sediment, besides single scolices with a double row of hooklets or remnants of these and single hooklets.

In *bilharzia haematobia* the pyelitis accompanies the cystitis. It is always complicated by copious parenchymatous hemorrhages. In the sediment we find numerous blood and pus-corpuscles, kidney and bladder epithelia, and coagula of fibrine enclosing the characteristic ova of the bilharzia. There is also present much albumen and blood-coloring matter, dissolved.

Para- or *perinephritis* can not be diagnosticated from the urine as the latter, even in a severe attack, frequently produces normal urine.

2. Hæmaturia.

Strictly speaking, this is a symptom and not a disease, but as it accompanies so many diseases and these diseases can not always be determined, we therefore having to be satisfied with the diagnosis "hæmaturia from unknown causes," we have thought it best to treat of it here.

Hemorrhages from the urinary apparatus may be divided into three classes:

a Hæmoglobinuria (hæmatinuria of Vogel);

b Parenchymatous hemorrhage, and

c Copious hemorrhage, produced by the rupture of large blood vessels.

1. Hæmoglobinuria is characterized by a reddish brown, brownish-black urine, from which, even after it has stood for hours, no red deposit forms. It retains its uniformly reddish brown color, because the blood-coloring matter is dissolved. The reaction is usually acid and sp. gr. diminished. It contains much hæmoglobine and methæmoglobine. In the sediment hemorrhagic epithelia and brown molecular detritus are sometimes found. Blood corpuscles are not present.

2. In *parenchymatous* hemorrhage, we also observe a reddish brown, frequently coffee-colored urine, which will retain its color for a long time, but deposits a reddish brown sediment, consisting of red blood corpuscles. Its reaction is acid, its sp. gr. varies, and it has dissolved hæmoglobine, more or less altered.

For the parenchymatous hemorrhage the sediment is characteristic. There are found, in it, blood corpuscles of various sizes. Frequently normal, round corpuscles, with depressions, cannot be seen at all, but in their stead they are globular, spherical and colored brown. Frequently they are entirely colorless, looking like small rings.

In the same field we will observe very large ones, others only are half or one-quarter as large as normal, and some as small as dust.

These microcytes, which, in modern times, have been observed so frequently in the blood of patients, have long ago been known to exist in the urine from parenchymatous hemorrhage, and have been considered as characteristic for it.

3. In the hemorrhage coming from the *rupture of large vessels*, the urine is either dark reddish-yellow or red, similar to venous blood. The reaction is, commonly, neutral or alkaline. The sp. gr. varies. The urine usually contains traces of coloring matter in solution; it is only when much ammonium carbonate is present, a rare occurrence, that considerable quantities are dissolved.

Usually the urine from rupture of large vessels deposits its entire blood, after standing for several hours, in the form of a copious red sediment in which the blood corpuscles appear of their normal color, size and shape.

Albumen can always be found in this kind of urine.

These three forms of hemorrhage may originate in the bladder, the pelvis or the kidney and we are not always so fortunate as to be able to state where the blood comes from.

1. We seek to utilize the reaction for the differential diagnosis. Generally, it is accepted that, in hemorrhage from the kidney, it is acid; from the bladder, alkaline. But this is not always the case; indeed, the one can only occur when hemorrhage is complicated by purulent catarrh of the pelvis or bladder. Here the reaction on litmus is not decisive, for, in large hemorrhages, we find the alkalinity of the blood neutralizing the acidity of the urine, and we may have an alkaline reaction even if the blood comes from the kidney. The internal administration of alkalies could be sufficient to make the urine alkaline or the amount of pus formed in the pelvis of the kidney, with its alkaline reaction, could be sufficient to neutralize the urine—in these cases we would have an alkaline reaction and yet the hemorrhage not from the bladder.

On the other hand, it cannot be denied that hemorrhages

from the bladder occur in which the reaction of the urine is acid. This is always the case when purulent catarrh of the bladder is absent and when the hemorrhage is not very great.

Of greater importance than the reaction is the detection of carbonate of ammonium. If this is present in sufficient quantity, then the likelihood of hemorrhage from the bladder becomes greater, especially if, at the same time, we find crystals of the triple phosphate in the sediment.

2. The color of the urine is of greater importance in this respect. The older practitioners have always associated the reddish brown or brownish black color of the urine with hemorrhage from the kidney and the light red with hemorrhage from the bladder. This, however, is not altogether correct. The dark colors are produced by decomposed hæmoglobine (methæmoglobine), and can only occur when blood has been intimately mixed with urine and retained within the body for some time. This occurs in parenchymatous hemorrhages: the blood is gradually mixed with the urine; the blood corpuscles remain, for a long time, in a comparatively large quantity of fluid containing substances undergoing retrograde metamorphosis; the constituents of the urine, therefore, have sufficient time to exert their destructive influence upon the red corpuscles, converting hæmoglobine into brown methæmoglobine.

For this reason the urine in parenchymatous hemorrhages, even when they come from the bladder (cancer), takes upon itself the brown tints.

It is an entirely different matter when the hemorrhage is produced by the rupture of larger vessels (hæmorrhoids of the bladder). Here a large quantity of blood is suddenly introduced into the bladder and suddenly dilates it. This is

followed by tenesmus and the blood is passed before the urine has had time to act upon the haemoglobine.

As hemorrhages from the bladder are, as a rule, produced by rupture of large vessels, and those from the kidney are parenchymatous, we can readily understand how the different color of urine becomes a very valuable diagnostic point.

3. The specific gravity is of importance in that, in hemorrhage from the kidney or pelvis, disease is usually present that produces polyuria; therefore low sp. gr., while in hemorrhages from the bladder, there is, as a rule, no change in this respect.

4. If *coagula* are present they sometimes point positively to the seat of the lesion.

If the coagula are soft and have the color and consistency of fresh, coagulated blood, then they have not existed for a long time; but if they are discolored, then they are old and have been retained for some time. Short, rod-like coagula sometimes come from the dilated pelvis (Simon) and are found after hemorrhages from the kidney; formerly they were considered as concrements made up of pure fibrine (Heller).

Large, irregular, shred-like coagula, are said to come from the bladder. We must call especial attention to the fact that the rod-like coagula alone can be considered of diagnostic value. If they are present we can state positively that the seat of hemorrhage is above the ureters, for the long coagula are molds of the ureters. The irregular coagula, on the other hand, are not at all characteristic. They may be produced in the pelvis as well as in the bladder.

It may even happen that fluid blood, poured out in the kidney, passes into the bladder and coagulates there.

Moreover, coagula are not constant in hemorrhages. Parenchymatous and copious hemorrhages will rarely produce coagula. They occur when the blood comes from vessels of small calibre.

5. The most important aid to diagnosis is afforded by the microscopic examination of the sediment.

For parenchymatous hemorrhages from the kidney, the so-called blood casts and hemorrhagic epithelium of the kidney are characteristic. After copious hemorrhages, however, (if occurring from large vessels,) these are not found. It is highly probable that kidney epithelia are present but they are covered over by the great number of blood corpuscles, and cannot be detected.

Hemorrhages from the bladder are frequently not at all characterized by the sediment. Sometimes we find an increase in epithelia from the bladder and crystals of triple phosphates.

After the description of the microchemical characteristics of hemorrhages from the urinary apparatus,we proceed to discuss the diseases in which they occur and also seek new diagnostic points.

I. *Haemoglobinuria* (with or without methaemoglobinuria,) occurs in the hemorrhagic diathesis, scorbutus, congestive chills, in putrid typhus fevers, in fact, in all diseases that are accompanied by blood dissolution; after the inhalation of arsenetted hydrogen, carbonic acid gas and other similar substances. Also, after transfusion with animal blood do we find haemoglobinuria, especially in those cases in which much blood has been used.

II. *Parenchymatous Hemorrhages* may come from any part of the urinary apparatus.

(*a*) Hemorrhages from the kidney, in addition to the diseases before enumerated, usually associated with haemoglobinuria, are found:

1. Occasionally, in acute febrile diseases, especially in the exanthemata, where the hemorrhage represents a higher degree of hyperaemia.

2. In the majority of cases of chronic parenchymatous nephritis.

3. As a rule, in atheromatous degeneration of the vessels of the kidney.

4. In thrombosis of the renal vein, occurring in general cachectic conditions; in puerperal fever, with phlebitis of the femoral and uterine veins; furthermore, accompanying serious injuries of the kidney, sometimes with traumatic nephritis; finally, as a result of compression by tumors in the neighborhood of the hilus.

In infants suffering with intestinal catarrh, thrombosis of the renal veins sometimes occurs. According to O. Pollak this is recognized by the children becoming jaundiced, by a great diminution of urine following, and in that we find in the sediment, blood casts, blood corpuscles and hemorrhagic kidney epithelium.

Hemorrhages from the kidney are furthermore observed:

5. Constantly in renal calculi, when severe pyelitis has not developed. The sediment, besides those elements characteristic of calculi, contains blood corpuscles and kidney epithelia.

6. In cancer of the kidney; besides the hemorrhage, nothing suspicious is found. We have never found cancer cells nor cancer tissue in the sediment, but such a thing may occur when the cancer grows into the pelvis of the kidney.

In small children there are observed large tumors of the size of a fist in the kidney without our being able to detect a sign of albuminuria. Haematuria, therefore, is not always present in tumors of the kidney, but is a very common symptom.

7. In nephrophthisis or in caseous inflammation of the kidney, of the pelvis, and the ureters. In addition to the microcytes, we find, in the sediment, kidney epithelium, pus cells, much molecular detritus, numerous vibriones and cocci; sometimes waxy casts, mixed with casts made up of bacteria.

(*b*) Hemorrhages from the bladder are observed:

1. In stone in the bladder and in catarrhal ulcers at the neck of the bladder. Haematuria is of a mild nature.

But in both cases microcytes can not be detected in the sediment. All the red corpuscles are of normal size. If catarrh of the bladder is also present then we find its characteristic urine.

Haematuria in vesical calculus becomes more intense after exercise and ceases when the patient is in bed. Haematuria in catarrhal ulcers, situated at the neck of the bladder, usually originating in gonorrhœa, takes place at the end of micturition when the sphincter of the bladder begins to contract.

2. In papilloma and villous carcinoma of the bladder, parenchymatous hemorrhages also arise from the papillomatous proliferations of its mucous membrane. Not infrequently we find in the sediment necrotic papilla tissue, which facilitates diagnosis. (See chapter on cancer.)

(*c*) Parenchymatous hemorrhages throughout the entire apparatus occur.

1. Sometimes, after the emptying of a paretic or paralyzed bladder with the catheter. If the entire urine is

drawn off, a quantity of which probably has remained for years in the bladder, because the paretic bladder was unable to pass it, an hyperaemia ex-vacuo must occur, which becomes the more intense the thicker the muscular coat of the bladder is, and the greater its inability for contraction. At the same time the pressure in the kidney is also changed, producing a parenchymatous hemorrhage.

2. They are also observed in Egypt, as a result of the bilharzia hæmatobia. Emboli of the vessels of the mucous membrane are produced by the ova of the distoma haematobium. The sediment is characteristic for this disease.

III. *Large hemorrhages after the rupture of vessels* only occur in tumors and varicose vessels at the neck of the bladder.

In tumors they only occur when the cancer has existed for a long time and begins to ulcerate. In the so-called hæmorrhoids of the bladder the bleeding is very profuse, coming on very suddenly and, after 1 or 2 days, rendering the patients very anaemic. It usually lasts for several days, then leaves the patient perfectly well, returning after months or years. In the sediment we only find blood corpuscles of normal size.

In diphtheretic and croupous processes of the bladder, occurring after dissolution of the blood, we also find blood in the fetid, ichorous and alkaline urine.

3. Cysto-Pyelitis and Pyelo-Cystitis.

Under this designation, a purulent catarrh affecting pelvis, ureters and bladder is understood. If the pelvis is principally affected it is cysto-pyelitis, but if it is the bladder then we term it pyelo-cystitis.

By characteristic signs we determine whether it is the bladder or the pelvis that is principally affected.

If pyelitis prevails, then polyuria will usually be present; the urine will be of neutral or faintly alkaline reaction; sp. gr. will be low, and the purulent sediment will not adhere to the glass. Albumen will be present in greater quantity than would correspond with the amount of pus present, and in the sediment we find pus corpuscles, kidney and bladder epithelium and crystals of the triple phosphate. The pus corpuscles are well preserved and sometimes united to form plugs.

If cystitis prevails, polyuria is absent; the urine is very alkaline, its sp. gr. normal or only slightly diminished. The sediment is pasty and adheres to the vessel. Albumen is present to corespond with mixed albuminuria and considerable quantities of ammonium carbonate can be detected.

In the sediment the pus corpuscles are very much swollen, lying between a great number of crystals of the triple phosphate; in addition we find single kidney and bladder epithelia.

Cysto-pyelitis and pyelo-cystitis occur frequently in stricture of the urethra, in hypertrophy of the prostate and in paresis or paralysis of the bladder.

In addition, from cystitis or pyelitis, cysto-pyelitis and pyelo-cystitis may easily originate by direct continuity of the tissues. It is not rare that cystitis alternates with pyelo-cystitis, and pyelitis with cysto-pyelitis.

The prognosis depends upon the cause and the prevailing disease.

(*c*) Forms of False Albuminuria.

False albuminuria is distinguished from the other forms by the fact that true albumen is present in quantities corre-

sponding with the quantity of blood or pus present in the urine. The albumen that is detected is albumen from pus or blood serum, and these disappearing suddenly, as after the rupture of an abcess or varix into the bladder, the albumen will also be gone.

We have seen from whence true and mixed albuminuria always comes: by exclusion we can arrive at the seat of lesion producing false albuminuria; the bladder, urethra and their adnexa.

1. Cystitis—Catarrh of the Bladder.

We have acute and chronic cystitis, and of each, three degrees.

In cystitis of the first degree, the urine contains neither pus nor albumen, but simply an increased amount of mucus and has an acid reaction. In the second degree it contains albumen and pus, has an alkaline reaction and a mucilaginous greenish sediment. The third degree is characterized by ichorous, fetid urine, the presence of much albumen, pus and blood, and a marked alkaline reaction; it occurs as a result of ulcerative processes in the bladder, and, not infrequently, has suppurative nephritis as complication.

In catarrh of the bladder the urine usually has an alkaline reaction, and many practitioners, even to-day, diagnosticate this form of disease by means of litmus paper.

This test is usually a reliable one, but then there are cases of cystitis in which the urine has an acid reaction. But this is only true for the urine when passed recently, for in a few hours it becomes alkaline.

(*a*) *Acute catarrh of the bladder of the first degree* presents the following:

The quantity of urine is not diminished. The urine has a normal or dark wine-yellow color and is turbid. The reaction is faintly acid, but changes in a few hours to alkaline. There is considerable sediment, very cloudy and not solid.

Excretion of normal constituents is unchanged.

Carbonate of ammonium is the only abnormal substance that can be detected.

The sediment consists principally of cloudy mucus. Microscopically we detect mucus corpuscles (young cells) and epithelia from the bladder, in small quantity. After a few hours small numbers of the crystals of the triple phosphate are found.

This form represents a diseased condition of the mucous membrane, as it occurs in prostatitis after gonorrhœa and after the introduction of instruments into the bladder and urethra.

(*b*) *Chronic Catarrh of the first degree* is characterized by a wine-yellow, exceedingly cloudy urine, whose sp. gr. is normal and whose quantity is not increased. The reaction of the fresh urine is acid but quickly becomes alkaline. The sediment is considerable and cloudy. Sometimes the urine has a peculiar penetrating odor and the cloudiness, consisting principally of bacteria, is never completely deposited.

The only thing abnormal in the solids is the presence of carbonate of ammonium in small quantities.

The sediment is the same as that of the preceding form, with the addition of bacteria.

This form of urine is found in patients that are forced to use the catheter in order to empty the bladder; in hypertrophy of the prostate gland, paresis of the bladder and similar obstructions to the passage of urine. In elderly

women, that have given birth to many children, or that suffer from any diseased condition of the uterus, this condition is nearly always present.

(*c*) *Acute catarrh of the second degree* is distinguished from the preceding forms principally by the amount of pus present in it.

The urine has a dark wine-yellow color and is turbid. The turbidity is produced by mucus and pus, while in the catarrh of the first degree, the cloudiness is produced by mucus alone. The quantity and sp. gr. are normal, but the reaction is alkaline. The sediment is greenish yellow and adheres to the vessel in which the urine is preserved.

The normal constituents are only changed in that part of the urea is changed to carbonate of ammonium.

Albumen is found in quantities to correspond with the amount of pus present, and carbonate of ammonium is present in great quantity.

The sediment consists of alkaline pus mixed with crystalline and amorphous earthy phosphates. With the microscope are detected blood-corpuscles, urate of ammonium and very much epithelium from the bladder.

This form occurs in hypertrophy of the prostate; after lithotripsy of large and hard calculi; after the dilatation of strictures; after catheterisation or the introduction of other instruments. Furthermore, after gonorrhœa and acute prostatitis, and, finally, after catching cold, especially depending upon the action of cold and moisture. In women, after operations upon the uterus or vagina, in perimetritis and pericystitis. Sometimes this form is also observed after the administration of cantharides or other medicaments. It is said that the drinking of badly-fermented, so-called "young" beer will also produce this disease.

(*d*) *Chronic Catarrh of the bladder of the second degree* produces urine that is nearly identical with that just described. In addition, as in the chronic catarrh of the first degree, we find bacteria in the urine.

In the sediment the pus corpuscles are very much swollen, their outlines indistinct and the nuclei distinctly visible: frequently, the latter alone are observed imbedded in an homogeneous, granular mass.

Sometimes the pus is entirely dissolved in the alkaline urine, giving to the latter a syrupy, tenacious consistency.

This form is found in hypertrophy of the prostate gland, in paresis of the bladder and in diseases causing obstruction to the passage of urine.

(*e*) *Acute catarrh of the third degree* includes those processes that have been called cystitis, parenchymatous and pericystitis.

Although we are not always able to diagnosticate these diseases from the urine, yet diagnosis is very much facilitated by its examination.

If the quantity of pus is very variable then we can sometimes deduce the rupture of an abscess of the bladder.

The urine presents the same changes as that of the second degree, with the exception that the purulent sediment does not adhere to the vessel and that it contains many blood corpuscles.

(*f*) *Chronic Catarrh of the third degree* is a purulent catarrh complicated by an ulcerative process in the bladder.

The urine is of a dirty brownish-yellow color, has a fecal smell, its reaction is strongly alkaline and the turbidity is produced by pus, mucus and bacteria. The sp. gr. is diminished; the sediment of the same color as the urine and adheres to the vessel.

The normal constituents are diminished:

Of abnormal constituents we find a great quantity of albumen, blood coloring matter, ammonium carbonate and ammonium sulphide.

The sediment consists of ammoniacal pus mixed with blood and earthy phosphates. With the microscope we find large quantities of bacteria, molecular detritus and single epithelia from the bladder.

This process occurs in paralysis of the bladder and great hypertrophy of the prostate gland. It is easily complicated by pyelo-nephritis or suppurative nephritis. Symptoms of uraemia or ammonaemia close the scene.

Similar urine is found in tuberculous ulcers of the bladder and in diptheria.

In croupous affection of the bladder, as they sometimes occur, especially in women, large reddish-white membranes, consisting of fibrine as discharged with the urine.

In practice, the symptoms of spasm of the bladder are frequently confounded with those of cystitis. Only the examination of the urine will make this diagnosis easy.

In *Spasm of the Bladder* the urine is usually clear, in case it is turbid, it is due to the earthy phosphates, amorphous and about to be deposited. Besides, the urine is pale and has faintly acid or neutral reaction.

In boiling, the urine becomes cloudy, earthy phosphates and carbonates are deposited, that are readily soluble upon the addition of a small quantity of acetic acid. Sometimes carbonate of sodium can be detected.

Albumen, pus, carbonate of ammonium, etc., are not present in spasm of the bladder.

In the sediment are found calcium carbonate, crystalline

calcium phosphate and amorphous earthy phosphates. Crystals of the triple phosphate and epithelial cells from the bladder are absent.

2. Neoplasms in the Bladder.

Having discussed the varieties of hemorrhage from the bladder under the head of "Haematuria," it now becomes necessary to state, in detail, the uroscopic signs found in the various kinds of neoplasms of the bladder.

We find the following:

(*a*) Simple fibrous polyps, with a pedicle and hanging into the bladder; they are very rare.

(*b*) Medullary sarcomata; also very rare.

(*c*) Epitheliomata and

(*d*) Villous, or vascular tumors.

1. *Fibrous polyps* produce symptoms of catarrh of the bladder of the second degree, and only when they ulcerate do we find blood in the sediment.

We are not able to diagnosticate this form of disease, as it does not cause any characteristic histological elements to appear in the sediment.

2. *Medullary sarcomata* produce a similar urine, except in the later stages, when they are followed by catarrh of the third stage. The urine is sometimes of a greenish-brown color and has a very offensive odor. In the sediment is found much molecular detritus, but nothing characteristic.

3. Epitheliomata usually develop very slowly, sometimes producing a catarrh of the second, sometimes of the third degree. The sediment always has more or less of a bloody tint.

Upon microscopical examination we sometimes find peculiar, numerous small epithelial cells (in addition to blood

and pus corpuscles) that sometimes are found in equally great numbers with the pus cells.

They are small, round or oval, not unlike kidney epithelium. Sometimes they are caudate or have two or three small processes. The nuclei occasionally are very large and several are visible in one cell. Ten or twelve of these cells adhere and then form ragged epithelial structures.

Although the diagnosis of epithelioma is not justified by this appearance, any suspicion that may be had regarding the nature of the disease is very much strengthened by this microscopical appearance.

4. *The papillary or vascular tumors* can always be diagnosticated from the urine.

Two kinds of this form of tumor can be recognized: 1, the papillary proliferations (papilloma) of the mucous membrane of the bladder, and, 2, the true villous cancer.

Parenchymatous hemorrhages are common to both forms; both forms are sometimes accompanied by catarrh of the second degree, sometimes of the third; in the first form only the papillomatous proliferations may necrose and fall off, the patient again being restored to health; in the second cachexia is developed and the patient dies.

The villous cancer is made up of a mass more or less soft, similar to medullary sarcoma tissue, growing into the posterior, inferior wall of the bladder, so that a thickening or tumor can be felt by the finger when introduced into the rectum. Upon this tumor, forming the surface, the peculiar villous tissue, which is made up of ecstatic capillaries and a covering of epithelium, proliferates

Papilloma of the bladder, on the other hand, is confined to the mucous membrane of the bladder. A tumor or thick-

ening of the walls of the bladder can not be felt from the rectum.

We cannot differentiate these two forms from each other by means of examining the urine—indeed, a villous cancer frequently develops from a papilloma. There are a few points that may make the differential diagnosis possible.

If we find villi, well developed, and covered over with a thin layer of epithelium, it is usually considered that a papilloma is present; if the layer of epithelium is so thick that the vessels within the villus can no longer be distinctly seen, then we assume that a cancer is present.

But this is of less importance than the detection of intumescence in the walls of the bladder and the presence of a cachexia.

On account of this difficulty of diagnosis it seems fit to discuss both forms together.

In these tumors the urine presents the following changes:

The quantity is not increased, the sp. gr. is normal. The color is that of parenchymatous hemorrhages, and the turbidity is produced by blood and pus corpuscles. The reaction is, usually, faintly acid; only when the tumor becomes larger and the cystitis more pronounced, followed by abundant suppuration, the reaction becomes alkaline. The sediment is flaky, brownish or brownish-red, and contains fibres or small ragged bodies of the same color.

The consistency of the urine is that of a thin fluid, but temporary fibrinuria is sometimes observed. This is the only disease that produces fibrinuria in our zone.

When passed, in these cases, the urine is thin, but in a few minutes congeals to a gelatinous mass that cannot be poured from the vessel. After shaking for some time the urine again becomes fluid and may then

be used for examination. Its color is not always blood-red, sometimes only pale reddish-yellow.

It is always accompanied by tenesmus. The fibrinuria can be explained by assuming that the blood vessels in the muscular layer are compressed by the violent cramp-like contraction of the muscular substance. The veins are compressed more than the arteries, and stasis takes place in the vessels of the villi. If the pressure is very great, rupture takes place, if not, the plasma of the blood is forced out, which afterward coagulates on account of the great amount of fibrine contained in it.

The normal constituents are unchanged:

Albumen and blood-coloring matter are frequently found in great quantity. We must especially notice the fact that the quantity of albumen is greater than would correspond with the quantity of pus and blood, due probably to increased pressure in the vessels. We must be careful not to make the diagnosis of disease of the kidney, in these cases, unless undoubted casts are found in the sediment. Small pieces of villi are apt to mislead the inexperienced observer, being looked upon as casts.

Ammonium carbonate can not always be detected.

When much blood or pus are present it becomes very difficult to see the cancer tissue—indeed, it is only by chance that particles are then observed. It is best, therefore, to select a comparatively clear and colorless urine for examination. Let the urine deposit its sediment and from this fish out the reddish flakes for microscopical examination.

The sediment consists either of blood only, or of blood mixed with pus. The blood is found in a fluid condition, but coagula are always found. The latter can be distinguished from the villous tissue by their dark red color. Not infrequently we find villous tissue inclosed in these coagula.

The blood corpuscles are the same as in parenchymatous hemorrhage.

The villous tissue may present itself in the most manifold forms, according to the reaction of the urine. We are disappointed if we think to find it as beautiful and characteristic as it is represented in text-books. Villous tissue, entire, living, does not occur in urine; it is only when we introduce a catheter that we occasionally find it adhering to the openings of the instrument. We usually find necrotic tissue in the sediment and this may vary very much in form.

In the beginning of the disease we find characteristic and beautiful villi [see fig. 14.]. The villi being necrotic and their blood vessels ruptured, we rarely find blood corpuscles whole in their interior. Beautiful villous tissue is found especially in papilloma of the bladder.

But we are not always so fortunate as to find this. Especially in cancer, with thick epithelial covering, it becomes impossible to discover the villi. The epithelial layer is beginning to necrose and the individual cells can no longer be discovered. It is infiltrated by pus and blood corpuscles and alive with bacteria. Sometimes branched structures are observed in this detritus that represent the stroma and the blood-vessels.

These histological points are not sufficient for diagnosis; but we find with the microscope, other bodies that make the diagnosis positive. They are as follows:

If we examine the necrotic tissue with high powers, we will find parts of the epithelial layer of a brownish color. If the urine is of acid reaction, a closer examination will reveal that these spots are made up of crystals of haematoidine. If a drop of fuming nitric acid is allowed to flow under the

thin slide, a change of color from green, blue to violet will take place. These crystals are characteristic of hemorrhagic tissue, and, in this respect, of importance for our diagnosis.

We also find peculiar crystals that are only found in the villous tissue, and therefore pathognomonic. They are small, colorless, round rosettes, that are dissolved in concentrate acid and alkalies only. They are probably oxalate of lime, as effervesce when treated as oxalate of calcium is in examining calculi.

If the urine is highly alkaline the villi are encrusted with urate of ammonium and the earthy phosphates. The patient then feels as if gravel were passing through the urethra, and usually demands an examination for stone.

3. Calculi of the Bladder.

If stones are present in the bladder we usually find blood in the urine, after exercise, that disappears again when the patient is at rest. The urine passed during the day is more bloody than that passed during the night, in contradistinction with other forms of haematuria where the blood is unchanged by time.

Calculi frequently cause cystitis. If they are small and smooth, as uric acid, for instance, they cause catarrh of the first degree. If the calculus is larger or possesses a rough surface (phosphates, oxalate), then it is accompanied by catarrh of the second degree. Hemorrhage into the bladder also depends upon the conformation of the surface.

The reaction of the urine depends upon the amount of catarrh present.

It is of importance to determine whether an affection of the kidney is also present [see "mixed albuminuria"]. If this

is detected it is probable that the same process is going on in the kidney as in the bladder.

Determination of the chemical composition of the calculus depends upon the chemical properties of the urine. The amorphous and crystallized combinations found in the sediment form the outer layers of the calculus. The nucleus, in the majority of cases, consists of uric acid (90%).

4. Diseases of the Urethra and the Prostate Gland.

These do not always produce marked changes in the urine. Acute and chronic prostatitis as well as hypertrophy of the prostate gland are usually complicated by catarrh of the bladder of the first and second degree. In prostatitis we usually have cystitis of the first degree; in hypertrophy, either of the first or of the second to correspond with the amount of retention of urine. When the prostata is very much hypertrophied we usually find spermatozoa in the sediment. It seems that the increase in glandular tissue compresses and destroys the muscular tissue of the ejaculatory duct, thus preventing its closure.

In *spermatorrhœa* the urine is either neutral or alkaline. Upon boiling it becomes cloudy and earthy phosphates are precipitated, dissolving upon the addition of acetic acid (Heller's bone-earth); albumen is not present. Besides numerous spermatozoa we find in the sediment, calcium carbonate, crystalline calcium phosphate and sometimes the triple phosphate. Before making the diagnosis it is necessary to know whether the urine has been passed immediately before an emission or coitus or not, as we always find spermatozoa in the urine after an ejaculation.

In acute and chronic *gonorrhœa* we find pus corpuscles and single cylindrical epithelia from the urethra.

If the urine does not permit the diagnosis of the origin of the pus, then it will be well to collect the urine in two vessels (Thompson). That passed first will contain all the pus from the urethra—that passed afterward will contain the secretions from the bladder or pelvis of the kidney.

The threads of gonorrhœa that may be found after normal cases of gonorrhœa, are commonly formed in the accessory glands of the urethra. It is only the very long threads, very rare, that may be formed in the urethra. These threads occur in two varieties—the one, thick, long and possessing at one end a head-like dilatation; the other, thin and short and without the dilatation. The former coming from the prostatic portion of the urethra, the latter from Littrés' glands.

Under the microscope they consist of pus corpuscles, mixed with cylindrical epithelia and imbedded in an homogeneous substance.

In croup of the urethra, small, white, membranous or tubular structures are passed with the urine, together with pus and blood.

END.